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Brit. J. Ophthal. (1957) **41**, 1.

COMMUNICATIONS

RADIOTHERAPY OF NON-MALIGNANT DISEASES OF THE EYE*

BY

M. LEDERMAN

From the Radiotherapy Department, Royal Marsden Hospital, and Moorfields, Westminster and Central Eye Hospital

RADIOTHERAPY has been used in the treatment of non-malignant disease of the eye for over 50 years; but progress in the development of this form of treatment has been hampered by its alleged dangers to the eye. It is true that in the early days ocular damage was frequently encountered, but the traditional view that the eye is readily damaged by radiation, was based upon early unsound experimental work, and the memory of the clinical disasters encountered by the pioneers. To-day this view can no longer be maintained, for with reasonable technical care and proficiency the radiation treatment of non-malignant disease of the eye should entail no risk of ocular damage either as a complication or as a sequela.

PURPOSE OF RADIOTHERAPY

In assessing the value of and indications for radiotherapy in non-malignant diseases of the eye, the purpose or object of this form of treatment must be clearly appreciated; otherwise the treatment may be misapplied, so that the patient is not benefited and the method itself becomes discredited.

(A) NON-NEOPLASTIC DISEASE.—In such cases the main aims of radiation treatment are:

(1) To relieve symptoms, particularly pain.

(2) To promote healing by assisting:
- (*i*) the resolution of inflammatory processes;
- (*ii*) the absorption of a haematoma or haemorrhage;
- (*iii*) the epithelization of an ulcerated surface;
- (*iv*) the organization and removal of granulation tissue.

(3) To affect blood vessels:
- (*i*) to reduce vascular engorgement and congestion accompanying inflammation;
- (*ii*) to obliterate or reduce in size newly-formed vessels invading the cornea.

(4) To reduce intra-ocular tension.

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(5) To restore function. *E.g.* an attempt may be made to improve vision where the cornea is the seat of an opacity, dystrophy, or degenerative process.

(B) NON-MALIGNANT TUMOURS.—In such cases radiation can be employed for the following purposes:

(1) To destroy a tumour for cosmetic reasons.

(2) To destroy or hasten the natural resolution of a tumour adjacent to and endangering the eye.

(3) To eradicate a precancerous condition.

The precise mode of action whereby radiation can favourably influence an inflammatory process is not known, but there are three possible mechanisms which may separately or together play some part in producing a favourable response (Pohle, 1950):

(1) A possible stimulation of antibodies.

(2) An effect on the cellular elements of the exudate, particularly the leucocytes.

(3) An effect upon the blood vasculature, especially the capillaries.

In the case of the benign tumours, the mode of action of radiation is by selective destruction of the tumour tissue, and it presumably differs in no fundamental way from the mode of action of radiation on other neoplastic processes.

INDICATIONS AND SELECTION OF CASES FOR RADIOTHERAPY

(A) INFLAMMATORY AND OTHER NON-NEOPLASTIC CONDITIONS

Whilst the exact mode of action of radiation in these conditions is uncertain and further speculation on this topic would be profitless, the fact remains that a sound knowledge of the clinical effects of radiotherapy and the purposes to which these can be put, provide a reasonable basis for selecting cases for this form of treatment. Table I (opposite) lists the non-neoplastic lesions, in the treatment of which experience shows radiotherapy to be of value.

It is obvious that only a minority of patients suffering from these diseases is likely to require radiotherapy, and an indiscriminate resort to this form of treatment is to be deprecated. Radiation is, after all, a noxious agent, its precise mode of action is still a matter for conjecture, and its effects are neither prompt nor certain. In these circumstances, any other methods of treatment known to give satisfactory results should always be given priority.

Whilst a hasty resort to radiotherapy is not to be recommended, undue tardiness is equally to be avoided. A patient failing to respond to recognized therapeutic measures within a reasonable time should not be deprived of possible help from radiotherapy, nor should he be left until the disease progresses to the stage when radiotherapy can only give symptomatic relief.

TABLE I

NON-NEOPLASTIC LESIONS

Inflammatory Processes	Pyogenic	Blepharitis
	Granulomatous	Tuberculosis Sarcoidosis
	Allergic	Vernal catarrh Phlyctenular kerato-conjunctivitis
	Viral	Superficial punctate keratitis Post-herpetic pain Dendritic ulcer Disciform keratitis Trachoma
	Unknown aetiology	Rosacea keratitis Marginal ulcerative keratitis
Miscellaneous	Corneal lesions	Ulcers (including Mooren's) Opacities following infection or trauma Dystrophies and degenerations (including pterygium) Traumatic lesions and recurrent erosions
	Epithelial downgrowths	
	Vascular abnormalities	Corneal vascularization (particularly after grafting) Eales's disease Retinal haemorrhage Venous thrombosis
	Raised intra-ocular tension	Secondary glaucoma

Radiotherapy should therefore be considered in the following circumstances:

(1) Where there is no response to recognized therapeutic methods within a reasonable time (1 to 2 months).

(2) Where no accepted method of treatment exists and there is reason to believe that radiotherapy may be of help.

(3) For chronic progressive lesions accompanied by symptoms which radiotherapy may relieve without necessarily arresting the course of the disease.

(4) For chronic relapsing lesions wherein periods of apparent improvement or healing are followed by repeated recurrence.

Of the conditions listed in Table I, the following are of most importance and interest to the radiotherapist:

(1) Mooren's ulcer.
(2) Rosacea keratitis.
(3) Corneal vascularization.
(4) Virus infections.
(5) Vernal catarrh.
(6) Pterygium.

(1) In cases of Mooren's ulcer, radiotherapy is the only method of treatment known to be of value (Fig. 1).

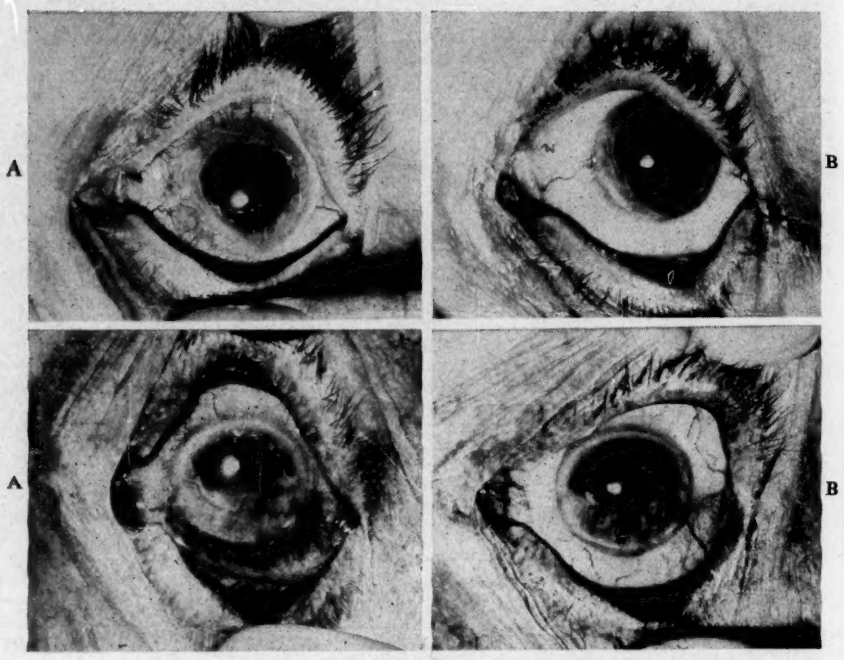

FIG. 1.—Mooren's ulcer in two patients.
A. Before radiation treatment. B. After radiation treatment.
(By courtesy of the Editors of the *British Journal of Radiology*.)

(2) There are very few remedies that can compare with radiotherapy in the treatment of rosacea keratitis, where radiation virtually proves itself the "morphia of the eye" (Fig. 2, opposite).

These two lesions are the sole exceptions to the general rule that radiotherapy should be used only as a last resort in the treatment of non-neoplastic processes. The early use of radiotherapy in Mooren's ulceration gives the patient his only chance of cure; in the treatment of rosacea keratitis, it gives the patient his best chance of avoiding loss of vision through the scarring that follows repeated attacks.

(3) The judicious use of radiation for corneal vascularization associated with keratoplasty can go far to help obtain a satisfactory functional result as in Fig. 3 (opposite) and Figs 4 and 5 (overleaf).

(4) In virus infections (Fig. 6, overleaf), and superficial punctate keratitis (Fig. 7, overleaf), radiotherapy is only occasionally curative, but it can nevertheless effect a certain degree of symptomatic relief not to be obtained by other remedies (Lederman, 1956b).

FIG. 2.—Rosacea keratitis.
A. Before radiation treatment. B. After radiation treatment.

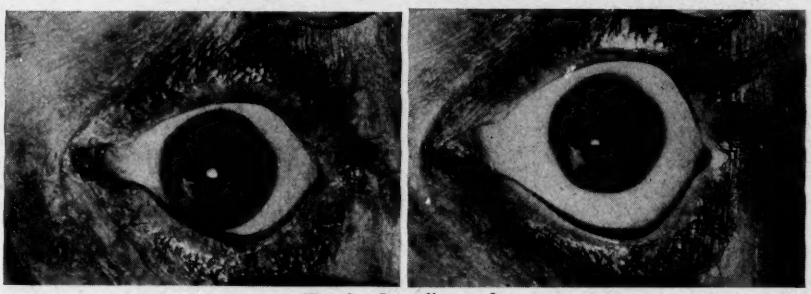

FIG. 3.—Lamellar graft.
A. Before radiation treatment. B. After radiation treatment.
(By courtesy of the Editors of the *British Journal of Radiology*.)

(5) A note of warning must be sounded in relation to the radiation treatment of vernal catarrh. It has been known for a very long time that radiotherapy can help sufferers from this condition, but in recent years there has been an enthusiastic revival of the beta-ray treatment of this disease, particularly in the United States. Although the sufferers are usually

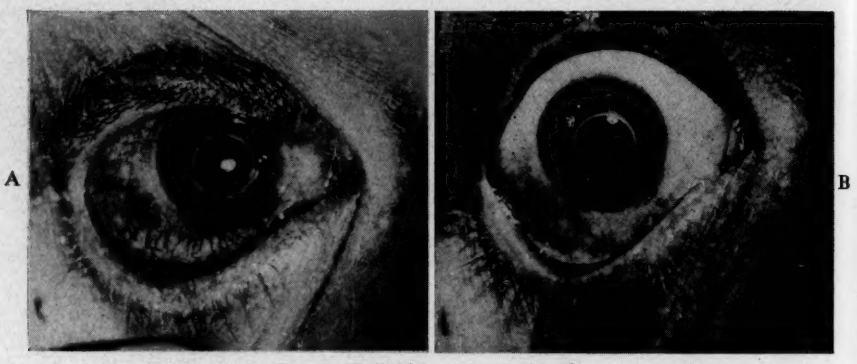

FIG. 4.—Full-thickness corneal graft.
A. Before radiation treatment. B. After radiation treatment.
(By courtesy of the Editors of the *British Journal of Radiology*.)

FIG. 5.A.—Disciform keratitis.
B. Full-thickness graft in association with pre- and post-operative irradiation.

children and the disease is seasonal and ultimately self-limiting, high doses of beta-radiation have been recommended as a method of eradicating the characteristic "cobble-stone" papules that appear on the tarsal conjunctiva. To any radiotherapist conversant with the effects of beta-radiation, the consequences of high doses applied to the mucosal surfaces of the lids could easily be predicted—namely, replacement fibrosis with atrophy and scarring of the palpebral conjunctival mucous membrane. Merriam (1956) has pointed out the risks of irradiating vernal catarrh in a recent paper on the effects on the eye of beta-radiation. He gives the following graphic account of the state of the unfortunate sufferers from this disease who have been misguidedly submitted to over-enthusiastic beta-irradiation:

> When the roughened keratinized surface (of the lid) rubs over the cornea, it produces a punctate keratitis with severe photophobia, lacrimation, and blepharospasm. This persists throughout the patient's lifetime, is resistant to treatment, and in our experience has been found to be much more debilitating than the disease originally treated. This possible effect should be given serious consideration before irradiation is advocated for a condition in which 90 per cent. of the cases subside spontaneously with local medication.

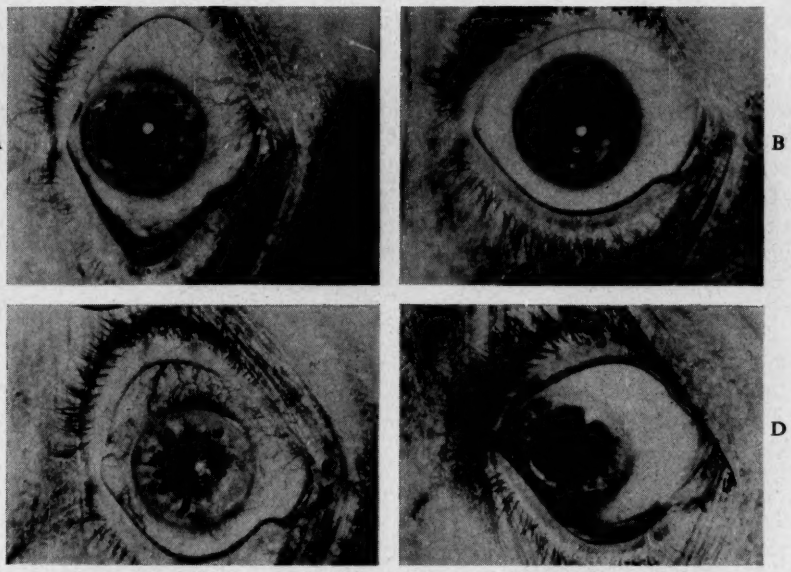

FIG. 6.—Dendritic ulcer. A. Before treatment. B. After beta-radiation. Second attack 5 years later. C. Before treatment. D. After beta-radiation.

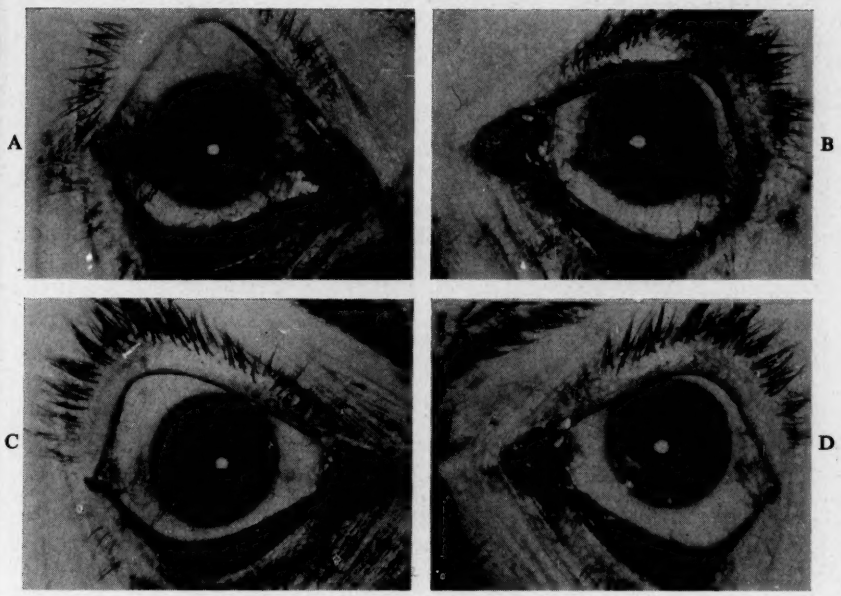

FIG. 7.—Bilateral superficial punctate keratitis.
A and B. Before treatment. C and D. After small doses of *x*-ray therapy.

The present writer has not practised the beta-ray treatment of vernal catarrh using high doses; after tentative trials, when it became obvious that the papules could not be eradicated with small safe doses, beta-radiation was virtually abandoned and small doses of *x*-radiation were used instead. The aim of treatment has been either prevention by irradiation one month before the expected onset of the seasonal attack, or reduction of the acuteness of the florid attack to relieve symptoms until the seasonal respite occurs. Beta-radiation is indicated only in the rare cases in which the bulbar conjunctiva is affected (Figs 8, 9, and 10).

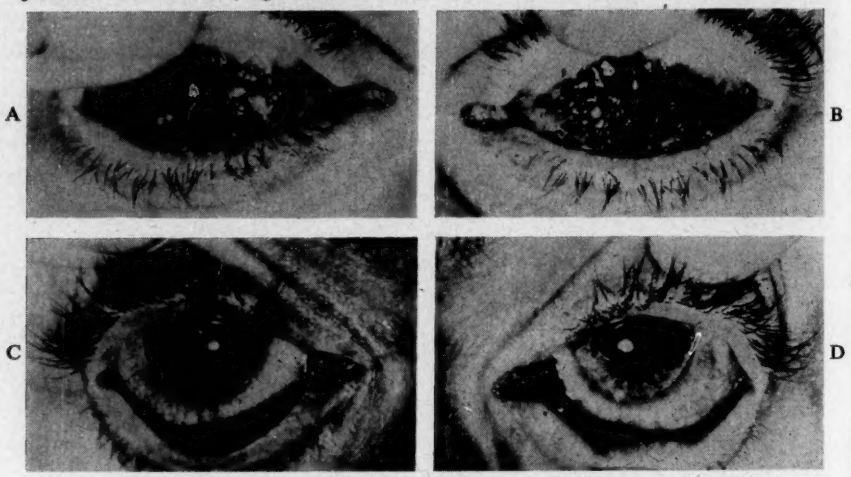

FIG. 8.—Vernal catarrh.
A and B. Typical "cobble-stone" appearance of lids
C and D. Associated corneal ulceration.

(6) Most of the cases of pterygium seen by the writer have been in patients coming from tropical and subtropical countries. The customary treatment is surgical removal, but the recurrence rate is by no means negligible. Radiotherapy should be reserved for the recurrent case, when excision and immediate post-operative radiation is the treatment of choice (Fig. 11, overleaf).

(B) BENIGN TUMOURS

The non-malignant tumours of the outer eye for which radiotherapy may be indicated are haemangiomata, papillomata, hyperkeratoses, and keloids. The need for and value of radiotherapy varies for each lesion.

(1) Haemangiomata.—It is probably true that most haemangiomata occurring in infancy disappear spontaneously without treatment. In spite of this, however, there are certain medical indications for active treatment:

(*i*) Presence of haemorrhage or infection.

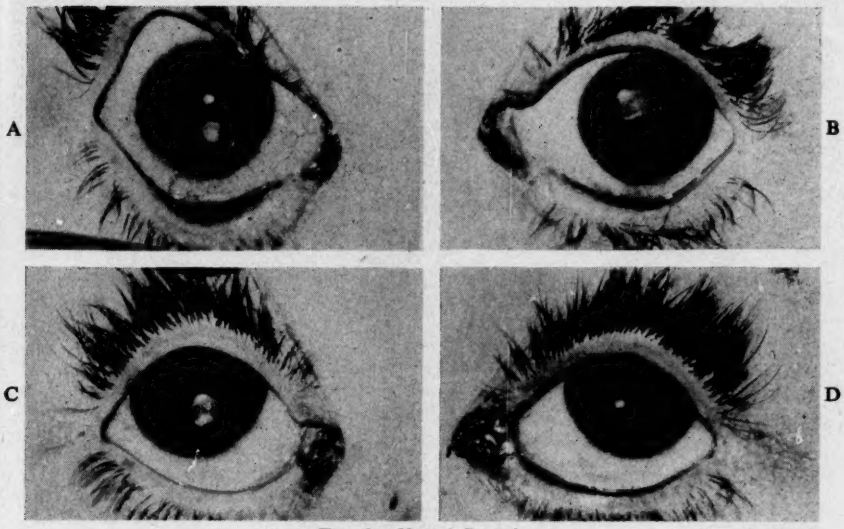

FIG. 9.—Vernal Catarrh

A and B. State of eyes before small doses of *x*-ray therapy—corneal damage is present.
C and D. State of eyes after treatment—the eyes are white and quiet and there has been relief of symptoms.

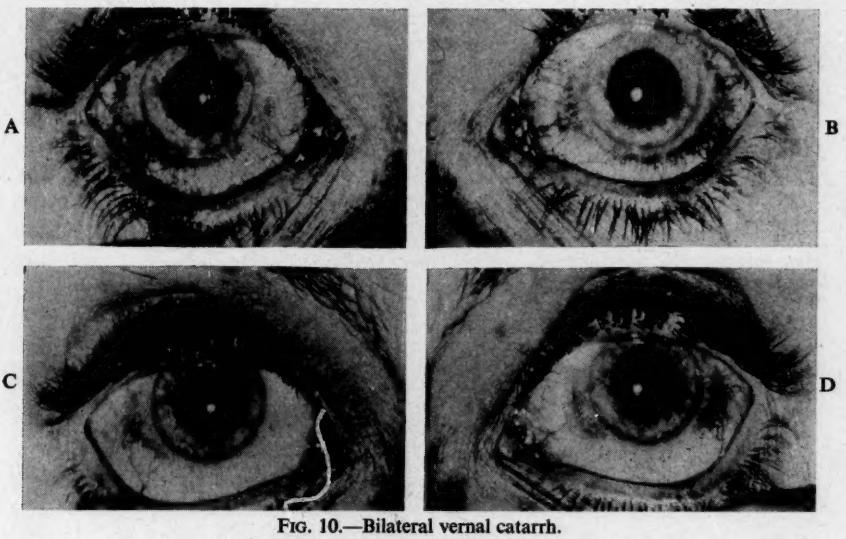

FIG. 10.—Bilateral vernal catarrh.

A and B. Bilateral bulbar vernal catarrh before treatment.
C and D. After beta-radiation—symptomatically improved.

FIG. 11.—Recurrent pterygia.
A. Before treatment.
B. After treatment.
Treatment was by surgery and immediate post-operative beta-radiation.

(*ii*) Situation of the haemangioma in a region exposed to frequent trauma, *i.e.* the scalp or the napkin area, or where its presence predisposes to infection of a neighbouring organ; *e.g.* infection may take place in the conjunctival sac where the lids are closed by an angioma.

In addition to these medical indications there is one further important indication; namely, the child is treated for the mother's sake. Many of the sufferers are first-born girl babies, and it is unreasonable to expect the mother to accept verbal reassurance that all will be well, particularly during the period when the angioma apparently increases in size with the growth of the infant. Radiotherapy is the treatment of choice for lid angiomata. There is no indication in these cases for excisional surgery which can only result in unnecessary mutilation and should be avoided at all costs. Radiotherapy offers a simple and safe remedy, the judicious use of which can arrest the growth of the angioma and restore confidence and peace of mind to the parents (Figs 12, 13, and 14, opposite).

(2) Papillomata.—The treatment of choice for either the true papilloma, or the infective wart is surgical removal. Such warts may be single or multiple and may affect the lids or the conjunctiva. It is rarely possible to cause true papillomata to disappear by using small safe doses of radiation, and an adequately effective dose of radiation must inevitably be accompanied

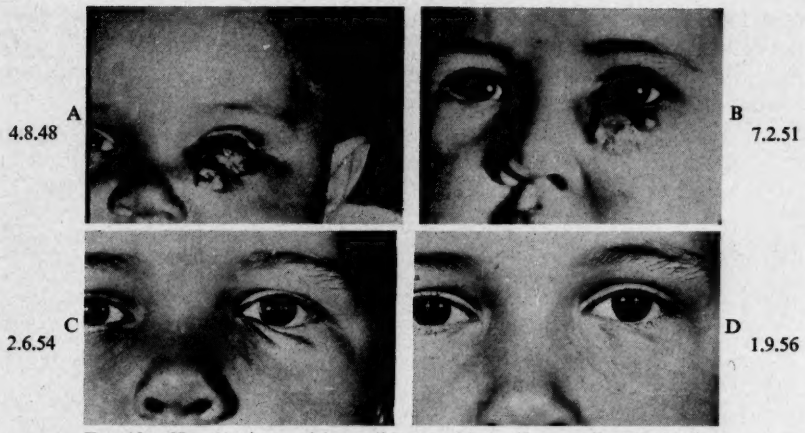

FIG. 12.—Haemangioma of lower lid treated by radium applicator showing rate of regression.

FIG. 13.—Haemangioma of upper lid.
A. Before radium treatment. B. 10 years later.

FIG. 14.—Haemangioma of upper lid.
A. Before radium treatment. B. 10 years later.

by a local tissue reaction. Such reactions occurring in regions away from the eye are reasonably free from risk, but in the eyelid or on the conjunctiva there are three special complications, the risk of which is real enough to contraindicate radiotherapy:

(*i*) Keratinization of the conjunctival epithelium of the treatment area. This occurs rarely but when it does it can be a serious matter, since, apart from producing an irritable eye, it may also damage the cornea (Fig. 15).

FIG. 15.—Papilloma of upper lid.
A. Before treatment. B. After treatment. The lesion has gone but there is keratinization of the lid conjunctiva in the treated area.

(*ii*) In the writer's experience a single-dose technique (2,000 r by L.V.T. 60 kV.) tends to produce a higher necrosis rate than fractionated techniques. The reason for using these single-dose techniques is their simplicity and economy, but radio-necrosis is a high price for a patient to pay for the treatment of a non-malignant lesion for which a safe surgical alternative is available.

(*iii*) The *x*-ray treatment of an epibulbar wart, particularly if situated near the limbus, may be followed by a radiation cataract. This risk can be minimized by the use of beta-radiation.

In spite of the desire to use surgery whenever possible, there are certain indications for radiotherapy in the treatment of papillomata:

(*i*) For a solitary sessile papilloma affecting more than one-third of the lid margin, when surgery would involve plastic repair of the lid (Fig. 15).
(*ii*) Multiple papillomata of the lids and conjunctiva (Figs 16 and 17, opposite).
(*iii*) Repeated recurrences after surgery.

(3) Keratoses.—The senile type of keratosis is usually a precancerous lesion and when affecting the lid margin is best treated by radiotherapy, because a wider area of tissue can be irradiated than can be excised. The need to irradiate or excise a wide area of tissue surrounding the lesion is due to the presumed "instability" of the tissues from which the keratosis arises.

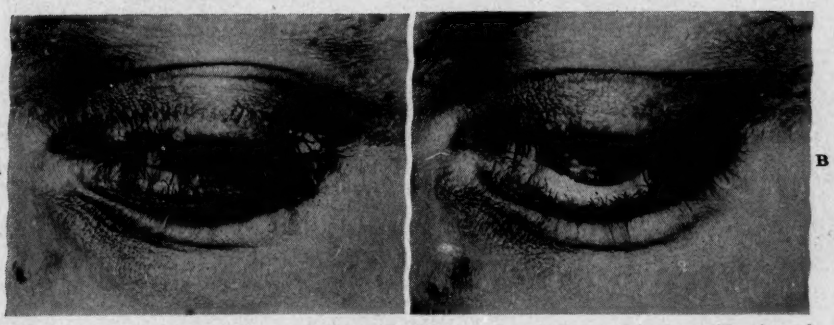

FIG. 16.—Multiple papillomata of the lids and bulbar conjunctiva treated by a combination of low-voltage *x*-rays to lid and beta-radiation to the bulbar conjunctiva.
A. Before treatment. B. After treatment.

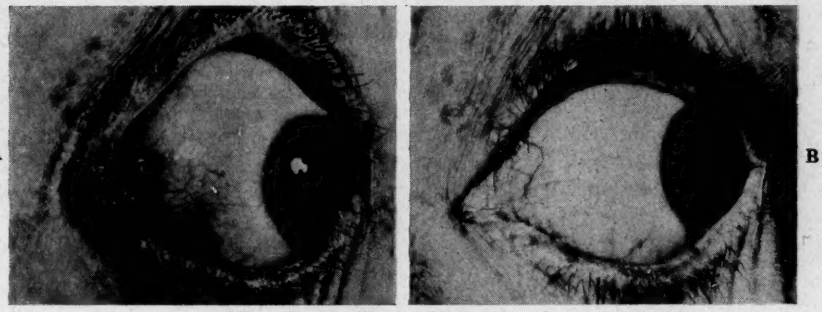

FIG. 17.—Papilloma of the conjunctiva.
A. Before radiation treatment. B. After radiation treatment.

(4) Keloids.—These may form in a scar on the lid, or may occur after injury or post-operatively. If the keloid is of the raised, red, fleshy type, radiotherapy should be undertaken, but if the lesion is of the hard, white, linear variety, excision associated with pre- or post-operative irradiation is indicated.

FACTORS INFLUENCING CHOICE OF TECHNIQUE

(A) NON-NEOPLASTIC LESIONS

The one factor which must dominate treatment is safety; in no circumstances must risks of damage be taken. Treatment can be made safe by attention to technical detail and utmost care in dosage.

The superficial situation and accessibility of the outer eye considerably simplifies apparatus requirements. With the exception of irradiation of the Gasserian ganglion for post-herpetic pain, which requires high-voltage therapy, all other non-neoplastic lesions can be treated by low-voltage therapy or beta-radiation, used either separately or in combination.

The particular method to be used chiefly depends on the acuteness and the extent of the lesion.

(1) Low-voltage therapy is *always* used for an acute or extensive lesion. The radiation is applied directly to the closed eye so that the whole of the outer eye and the eye-ball are irradiated.

(2) Beta-radiation is reserved for chronic lesions, chiefly affecting the cornea. Beta-radiation is not used in the presence of:

(*a*) severe lid spasm,

(*b*) a small pupil, marked ciliary congestion, or other evidence of uveal irritation or inflammation.

In the presence of lid spasm, any difficulty in inserting the beta-ray shell into the conjunctival sac may result in injury to the cornea, and the strontium beta-ray dose delivered to any co-existing inflammatory process deep to the cornea might prove excessive and produce an exacerbation of symptoms.

(3) Quite frequently, *x*- and beta-radiation may be used in combination. Thus, for an acute kerato-conjunctivitis or a deep keratitis associated with an iridocyclitis, treatment can be begun with low-voltage therapy and when the eye is reasonably comfortable and white, beta-rays can be applied to any persistent localized corneal lesion.

The effect desired from the treatment governs the selection of the particular radiation and dosage used. The purpose of the *x*-ray treatment is to assist the resolution of an acute inflammatory process affecting a part or the whole of the eye. The radiation is, therefore, applied in very small doses to the affected organ in its entirety on the assumption that the favourable effect of the radiation mediates through the blood supply, all of which should therefore be exposed to the radiation. In the case of beta-radiation, the "anti-inflammatory effect" of radiation is not usually sought, but the purpose is to heal a corneal ulcer or obliterate unwanted blood vessels invading the cornea; to achieve this, the strictly localized effects of high doses of beta-radiation are ideal.

There are two standard techniques for treating non-neoplastic lesions of the eye.

(1) *X-Radiation: Bulbar or "Whole Eye" Technique.*—This is so-called because no attempt is made to protect or shield any part of the globe or lids, treatment being given through a 3-cm. diameter circular field placed directly over the closed lids. The apparatus used has the following factors: 45 kV., 2 mA.; filter 1 mm. Al; focal-skin distance 4 cm.

The *x*-ray dosage employed in the treatment of an infection of the outer eye is always minimal, namely 10 r, and it would appear that, if radiotherapy is going to help, this minute dose is perfectly adequate. In my experience, there is no advantage in giving higher doses as, for example, of 100 r: the results are the same; the smaller dose is absolutely safe, does not provoke exacerbations, requires no manipulation of the lids, and can be continued for more than a month with safety. In the event of a relapse, a course of low-dosage treatment can be repeated two or three times a year.

X-ray treatment is given once or twice a week for 4 weeks, and the treatment can be stopped if the eye is comfortable and quiet at the end of this period. If the eye is white and corneal ulceration persists, beta-radiation can be used; if no improvement is observed, radiation treatment should be abandoned completely.

(2) *Beta-Radiation.*—This forms the mainstay of the treatment of corneal lesions. The apparatus comprises a plastic shell containing radio-active strontium foil (Lederman, 1956a). The shell is inserted into the conjunctival sac so that the radio-active surface comes into contact with the cornea and the surface of the globe. A range of such shells is available (Figs 18 and 19).

FIG. 18.—Radio-active strontium beta-ray applicator in place in conjunctival sac.
(By courtesy of the Editors of the *British Journal of Radiology*.)

FIG. 19.—Radio-active strontium beta-ray applicators showing range of applicators available.
(By courtesy of the Editors of the *British Journal of Radiology*.)

The dosage required depends on the lesion being treated.

For Mooren's ulcer single doses of 500 to 1,000 r are given at weekly intervals for 4 weeks.

For corneal ulceration of dendritic or rosacea origin a dose of 500 r is given weekly.

For corneal vascularization after grafting treatment may be begun 10 to 14 days after operation, and 500 to 1,000 r are given weekly for 4 weeks. The dose and the type of applicator used depend on the state of the eye when seen, and the extent,

age, and depth of the vessels to be treated; the treatment is the same whether the graft be lamellar or full-thickness. For pre-operative corneal irradiation, doses of the order of 500 to 800 r weekly are given for 2 to 4 weeks, and operation is advised 10 to 14 days after the last treatment. Pre-operative radiation can be followed by post-operative treatment in the more heavily vascularized cases.

For vernal catarrh, the patient should ideally be treated one month before the expected onset of the attack. A lead shield is placed in the conjunctival sac to protect the eye and the size of field used will depend on whether one or both lids are to be treated, in each case the fornices must be irradiated and the field extended to the bony orbital margin. A dose of 100 r is given once weekly for 4 weeks. If the patient is seen during an attack, the same treatment should be given. It is advisable when treating any bilateral eye condition to begin by treating the worse eye first and to treat both eyes only if no exacerbation of symptoms has occurred. For bulbar lesions, beta-radiation should be used in order to avoid lens damage, a dose of 500 r being given once a week for 4 weeks.

Recurrent pterygium can be treated by beta-radiation using the strontium shell, four doses of 500 to 600 r being given at weekly intervals. It can also be treated post-operatively by low-voltage *x*-rays (60 kV.) given through a 2 × 1-cm. field, so placed that its edge is at the apex of the pterygium and tangential to the cornea. The eye is anaesthetized and a lid-retractor is used. A single dose of 600 r is given, and this can be repeated after 6 weeks if necessary.

The doses used in beta-ray therapy bear little relation to the doses employed in low-voltage *x*-ray therapy, for the following reasons:

(*i*) The marked difference in penetration of the two types of radiation. Under our treatment conditions, the dose of *x*-radiation incident on the anterior surface of the lids falls to half its intensity at a depth of 1·1 cm. In contrast, the dose of strontium radiation incident on the surface of the cornea falls to half its intensity at a depth of 1·3 mm.

(*ii*) The volumes of tissue irradiated by each method vary greatly. With low-voltage therapy the lids and the eye itself are irradiated, whereas with beta-radiation only tissues in close contact with the source are irradiated. There is an inverse relationship between the volume of tissue irradiated and the size of the dose, *i.e.* the larger the volume the smaller the dose that can be safely given.

Any attempt to imitate the high single doses used in beta-ray therapy with low-voltage *x*-ray therapy would almost certainly be harmful to the inflamed eye. Conversely, to imitate the small doses used in *x*-ray therapy with a beta-ray source would be pointless and ineffective.

(B) Benign Tumours

(1) Haemangiomata.—It is our general policy:

(*i*) not to give large doses of irradiation to these tumours;
(*ii*) to avoid radon seed or other implantation methods;
(*iii*) to repeat treatment only once or twice with the longest possible intervals between treatments.

Gamma-radiation is to be preferred, but, because of the greater ease in protecting the eye, contact therapy (60 kV.) is usually employed for lid angiomata, and the child is anaesthetized for the treatment in most cases. A single dose of 250–400 r is given, depending on the age of the patient and the thickness of the lesion, the lower dose never being exceeded in a newborn infant. The treatment is not repeated as long as regression continues, but if the improvement is not maintained a further treatment is given after 6 months, and very rarely a third treatment after 18 months. The child should be treated as soon after birth as possible and the parents warned that complete regression may not be obtained for from 3 to 5 years or more (Fig. 12).

(2) Papillomata.—*X*-ray therapy is used for a solitary papilloma, a single dose of 2,000 r at 60 kV. being given. Infective or multiple papillomata in children are treated by *x*-ray therapy to the lid lesions, a single dose of 600 r being given, and beta-ray therapy to any bulbar conjunctival lesion, a single dose of 1,000 r being given. These doses can be repeated at the end of 3 months if necessary.

(3) Keratoses.—The technique is the same as for solitary papilloma.

(4) Keloids.—A single dose of 600 r, using *x*-rays at 60 kV. or 100 kV., is given to the scar and treatment is repeated in 3 months if necessary.

Complications of Radiotherapy

Complications should not be encountered in the radiation treatment of inflammatory processes.

(1) Exacerbation of symptoms during radiotherapy is nearly always a sign of improper dosage; in using *x*-ray therapy, the minute doses given never provoke exacerbations such as may occur with higher doses.

(2) Infection and traumatic damage to the eye may occur when using beta-rays, but with proper care these complications are entirely avoidable. Merriam (1956) has reported on the occurrence of radiation cataract after strontium beta-radiation. He notes that damage to the lens can occur only with very high surface doses. There are no indications for very high beta-ray dosage, *i.e.* over 4,000 to 5,000 r, in the treatment of non-neoplastic disease, and to date we have no record of a radiation cataract produced by beta-rays.

(3) Radionecrosis has occurred only after the single-dose method of treating lid tumours. A fractionated dose method is clearly preferable if radiotherapy is to be used safely rather than economically.

Summary

In assessing the value of radiotherapy in the treatment of non-malignant disease, it is important to remember the following facts:

(1) Radiotherapy is not a specific remedy.

(2) Many of the lesions treated are normally capable of spontaneous healing, but may relapse in a certain unknown proportion of cases.

(3) Radiation is often used only when all else has failed and patients often come with a chronic long-standing lesion or in an acute " resistant " stage.

(4) Because of the benign or self-limiting nature of many of the conditions treated, routine follow-up is not undertaken. A detailed statistical analysis of results, such as is available in the treatment of malignant diseases, is scarcely indicated.

Tables II to VIII show the results of treatment obtained at the Royal Marsden Hospital in a series of cases of various kinds.

TABLE II
HAEMANGIOMATA AND PAPILLOMATA

Condition		Seen	Treated		Not Treated
			Improved	Failed	
Haemangiomata ...	Lids	50	45	2	3
	Canthi	7	4	—	3
Papillomata ...	Lids	41	27	3	11

TABLE III
VERNAL CATARRH

Seen	Treated		Not Treated
	Improved	Failed	
21	15	2	4

TABLE IV
VIRUS INFECTIONS OF THE OUTER EYE

Infection	Seen	Treated			Not Treated
		Relieved	Improved	Failed	
Dendritic ulcer	22	3	10	7	2
Disciform keratitis	17	3	7	6	1
Post-herpetic pain	11	2	3	6	0
Superficial punctate keratitis ...	73	12	44	12	5

By courtesy of the Editors of the *Transactions of the Ophthalmological Society of the United Kingdom.*

TABLE V
ROSACEA KERATITIS

Treated	Healed	Improved	Failed or too Recent
101	25	68	8

TABLE VI
MOOREN'S ULCER

Treated		Healed	Improved	Failed or too Recent
Patients ...	34	11	10	13
Eyes	45	15	14	16

TABLE VII
PTERYGIA

Seen		Treated			Not Treated
		Successful	Improved	Failed	
Patients ...	12	3	7	3	6
Eyes ...	19				

TABLE VIII
CORNEAL GRAFTS

Radiation Treatment	Number Seen		Satisfactory		Failed		Indeterminate	
	Patients	Eyes	Patients	Eyes	Patients	Eyes	Patients	Eyes
Post-keratoplasty	67	70	21	22	22	23	24	25
Lamellar ...		26						
Full-thickness...		44						
Pre-keratoplasty...	18	19	2	2	10	10	6	7
Pre- and Post-keratoplasty ...	5	7	2	2	2	3	1	2
Total ...	90	96	25	26	34	36	31	34

I am indebted to the members of the staff of the Moorfields, Westminster and Central Eye Hospital and of the Royal Eye Hospital for sending most of the cases, and for their co-operation in treatment. I am grateful to the Editor of the *British Journal of Radiology* for permission to reproduce Figs 1, 3, 4, 18, and 19, and to the Editor of the *Transactions of the Ophthalmological Society of the United Kingdom* for permission to publish Table IV.

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THE AMORPHOUS SUBSTANCE IN THE TRABECULAR MESHWORK*

BY

F. VRABEC

From the Pharmacological Institute, University of Uppsala, Sweden, and the First Eye Clinic, University of Prague, Czechoslovakia.

VIRCHOW (1910), in his description of the micro-anatomy of the trabecular meshwork, mentioned the presence of some unfamiliar tissue-element in addition to the known structures. In the trabecular meshwork of the horse he observed fine threads originating and terminating in the endothelial cells, and running through the empty spaces of the meshwork. I have found no other description of this substance in the subsequent literature on the morphology of the trabecular system.

In working on the problem of the innervation of the trabecular meshwork (Vrabec, 1954), I have very often noted a similar picture. As my sections were mainly cut on the freezing-microtome, the conservation of the tissue components was better than in paraffin sections. In flat preparations of the trabecular meshwork, thin sheets of a perfectly transparent substance were very often seen. Their existence was indicated only by the presence of silver deposits. Even in frozen sections, however, it was not possible to explore this substance in detail, as it was not found in meridional sections. A systematic search for a better method of embedding was therefore made. Paraffin infiltration causes great deformation and celloidin was also found to be deleterious to this delicate tissue component. Many other methods were tested with little success. At the instigation of Prof. J. Wolf of Prague, Celodal-embedding was then tried. This method was introduced by Hoepke (1939), and is described in the text-book of microscopical technique by Romeis (1943). It causes only minimal changes in the amorphous substance, but the main disadvantage of the method is that once it is polymerized Celodal cannot be removed from the sections by any solvent, and it takes up some colour.

Material and Methods

Sheep's eyes were dissected equatorially, and fixed in 10 per cent. formol for a week. The anterior segment was then rinsed for 12 hrs in tap water, and the lens removed care-

* Received for publication October 26, 1956.

fully from behind. Next the anterior segment was dehydrated for 24 hrs in 50 per cent. ethanol, and after dehydration it was divided into four quadrants. One quadrant was embedded in paraffin as a control; the other three were placed in a mixture of 50 ml. 70 per cent. ethanol, 50 ml. Celodal*, 5 ml. 40 per cent. formol, and 1 ml. 25 per cent. w/v aqueous solution of ammonium chloride. The pieces remained in this mixture for 2 days and were then transferred to the definitive embedding mixture of 100 ml. Celodal, 5 ml. 40 per cent. formol, and 2 ml. ammonium chloride solution. This mixture was allowed to polymerize in a Petri dish for 2 days. After this time, it was firm enough to allow blocks containing the pieces of tissue to be cut. Polymerized Celodal is transparent, and exact orientation of the pieces is very easy. The blocks were then fixed on wooden supports with a few drops of a mixture of Celodal and ammonium chloride, and allowed to remain at room temperature. In a few days they had hardened to a suitable consistency. Such blocks can be cut in a similar manner to celloidin blocks, using an oblique knife, and the sections can be removed and stored in 60 per cent. ethanol.

Our sections were 15 μ thick, but 10 μ sections can easily be cut from such material.

Staining.—1 or 2 hrs in a 1:1000 solution of cresyl violet (Grübler-Hollborn) in distilled water. The embedding medium is only slightly stained.

Mounting.—Permanent preparations are difficult to make by this method, because mounting in Canada balsam causes the metachromasia to disappear, and the colour substance soon diffuses out of the section into the mounting medium. The use of glycerol gelatin conserves the metachromasia, but even such preparations deteriorate in a few months, and the endothelial cells and their nuclei deprive the amorphous substance of dye.

Findings

In the sheep's eye all the spaces between the trabeculae seemed to be filled by an amorphous substance staining a reddish violet. In the meshes of the uveal trabeculae no appreciable amount of this substance was found. Although the substance did without doubt stain metachromatically, its colour was quite different from the very reddish metachromasia of the corneal stroma (Fig. 1, overleaf). The collagen bundles of the sclera stained faintly pink, but the trabeculae appeared unstained probably by contrast with the compact coloured substance (Fig. 2, overleaf). The ciliary muscle following the trabecular meshwork took on an intensive, more bluish tone. The endothelial cells were practically invisible against the great amount of amorphous substance, but in thin sections or older preparations, they could be seen as a very thin, darkly-coloured lining of the colourless trabeculae.

We compared Celodal and paraffin sections, stained with cresyl violet and mounted in glycerol gelatin. The result is clearly shown in Figs 3 and 4 (overleaf). After embedding in paraffin a considerable shrinkage of the amorphous substance takes place, resulting in the formation of empty spaces. The endothelial cells remain close to the trabeculae, and only very fine threads run between the distorted layers of tissue. The concentration of amorphous substance is highest at the tip of the trabecular meshwork close to the cornea. The next highest concentration is in the external layers of the meshwork close to the inner surface of the sclera. The innermost layer of

* Celodal, a product of Bayer, Leverkusen, is a clear, thick liquid which polymerizes after the addition of acidic substances. All the instruments and dishes must be rinsed immediately after use.

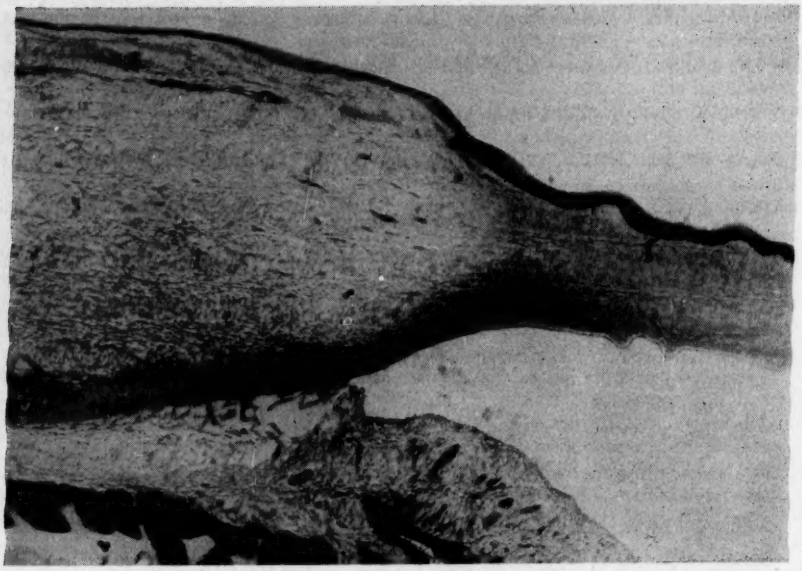

FIG. 1.—Meridional section of the chamber angle of the sheep's eye. Celodal embedding, cresyl violet stain. Metachromasia of the corneal stroma, intensive staining of the scleral meshwork, and very faintly coloured sclera. The uveal meshwork does not contain any coloured substance. ×50.

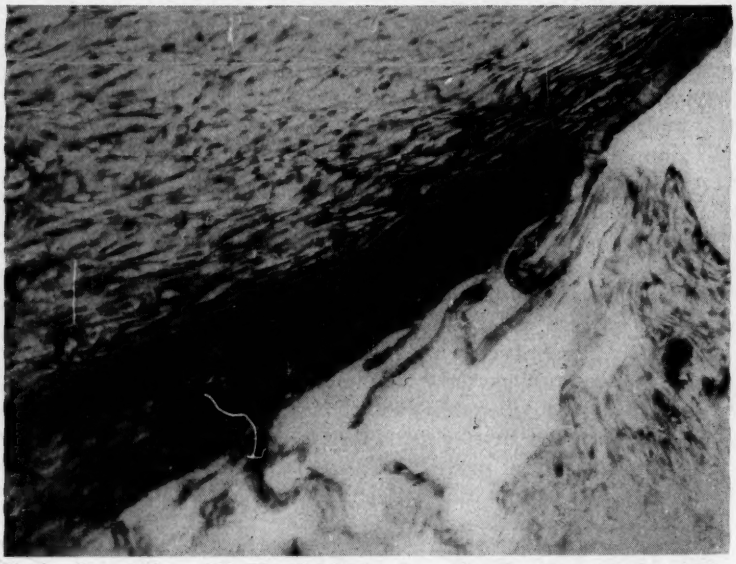

FIG. 2.—Same section ×200. The scleral trabecular meshwork appears strongly stained.

FIG. 3.—*Detail of tip of scleral meshwork of same section, showing great accumulation of amorphous substance in this region.* ×400.

FIG. 4.—Same region of scleral meshwork of same eye after paraffin embedding. All other staining and mounting manipulations were identical with those used in Fig. 3. The amorphous substance appears to have shrunken to fine threads, some of which are visible near arrows. ×400.

scleral trabeculae come next, and the middle layers of the meshwork are the palest.

The metachromatic material can also be seen in non-embedded preparations. On staining (with a 1:1000 solution of toluidin blue in water) a very thin, teased-out strip of the scleral meshwork of the formol-fixed cow's eye a very distinct metachromasia of the meshwork can be seen.

Discussion

The anatomical demonstration of the existence of an amorphous substance in the spaces of the trabecular meshwork confirms the physiological evidence provided by the work of Bárány (1956). It should be mentioned, however, that the human trabecular meshwork has been seen to stain metachromatically by Persson (1954) and by Berggren (1956), but these authors were not able to study the actual localization of the metachromatic material since they used only the classical embedding media.

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THE MUCINOUS LAYER COVERING THE CORNEAL ENDOTHELIUM IN THE OWL *STRIX ALUCO**

BY

ERNST BÁRÁNY, LENNART BERGGREN, AND FRANTIŠEK VRABEC

From the Pharmacological Institute, University of Uppsala, Sweden, and the First Eye Clinic, University of Prague, Czechoslovakia

ABELSDORFF and Wessely (1909) reported the curious observation made in connexion with other work, that the aqueous humour of certain owls, *Strix aluco* (*Syrnium aluco*, Tawny owl), *Athene noctua* (Little owl), and *Asio otus* (*Otus vulgaris*, Long-eared owl), is slimy and highly viscous and easily spun into threads. On acidification with acetic acid, a ropy precipitate is formed. The part of the aqueous close to the cornea seemed to be the most viscous, since the first portion obtained often blocked the needle. In young birds, the aqueous was not slimy.

The findings of Abelsdorff and Wessely are interesting for two reasons. First, it is difficult to see how an adequate circulation of this viscous aqueous could take place. Secondly, the presence of so much mucinous substance in the aqueous of one group of birds is of interest in view of the presence of muco-polysaccharides of unknown origin in the outflow barrier of eyes with normal aqueous. We have therefore repeated and extended the observations of Abelsdorff and Wessely on the eye of *Strix aluco*.

Methods

Five tawny owls were obtained from dealers and other sources. They each weighed about 400 g. Their age was not known. They were fed albino mice or rabbit meat.

In vivo observations of the eyes were made under anaesthesia with allylisopropylbarbituric acid,† 50–60 mg./kg. bodyweight given into the muscles of one leg. This dose induces a deep anaesthesia but allows full recovery. The observations were made with a Hamblin slit lamp and a Zeiss stereo-dissecting microscope (×6 to ×40).

For photographic purposes the living birds were unsuitable. Some experiments were therefore made with enucleated eyes. It turned out, however, that, because of the peculiar anatomy of the owl's eye, the process of enucleation caused an undesired mixing of the contents of the anterior chamber. Photographic experiments were therefore made with the eye *in situ* in the orbit. Some of these were done with the eye and its orbital cage immersed in saline in a cuvette of methylmethacrylate.

Viscosimetry was performed in microviscosimeters according to Cannon and Fenske (1938). The aqueous was diluted with barbital buffered saline, pH 7·2, containing a trace of diethyldithiocarbamate to remove heavy metals which might cause unspecific oxidative breakdown of hyaluronic acid after removal from the eye. The diluted aqueous was shaken for several hours and then centrifuged carefully. The enzyme used was a commercial staphylococcal hyaluronidase.‡

* Received for publication October 26, 1956.

† Numal(R) Roche.

‡ Hyason(R) from Organon, Oss, Holland.

Fluorescent oil with a refractive index close to that of water was made by dissolving a minute amount of "Fluorescent Green H.W. 187 per cent."* in petroleum ether, boiling point 40–60°. The dye is completely insoluble in water and stays in the oil.

Results

Subjective Observations on Living Eyes of the Owl.—Observed with the slit lamp, the intact anterior chamber is optically empty. There is no suggestion of a vitreous-like structure.

Sodium fluorescein injected into a leg soon appears in the anterior chamber, but it takes a long time for the chamber to become homogeneously fluorescent. Fluorescent clouds form and change only very slowly. Obviously, mixing is a much slower process than in ordinary eyes.

If a needle is pushed through the limbus in the plane of the iris and the tip is brought into the pupillary area, one can see how the needle-tip carries along threads of previously invisible material. If small air-bubbles are injected into the anterior chamber with the eye facing up they rise quickly towards the cornea. The smallest ones do not rise all the way, however, but become stuck below the cornea, at an estimated depth of 4 to 5 corneal thicknesses. Larger air-bubbles rise further. The surface of the bubbles soon becomes visible as if some dust had accumulated upon it.

These findings confirm the impression of Abelsdorff and Wessely that there is a gradient of viscosity within the anterior chamber of the owl, the more viscous layer being closer to the cornea. It seemed possible therefore that the circulation of the aqueous takes place mainly close to the lens and iris. In order to test this possibility a small amount of Indian ink was deposited close to the centre of the pupil, by means of a fine needle through the limbus. The ink spread instantaneously like a thin sheet over the iris, extending to the chamber angle. Obviously, the fluid along the anterior surface of the iris is much more mobile than that close to the cornea. It can be mentioned that the surface of the black fluid appeared silvery white, as if something had condensed on it.

Photographic Experiments.—These were performed on dead birds, in one case on the morning on which the bird had been found dead in its cage, in the other cases shortly after killing by decapitation.

Into one eye, held with the vertex of the cornea upwards, a small amount of homogenized cream was injected into the posterior chamber through a needle introduced at the posterior pole of the eye. In the owl, this is accessible without enucleation. The cream appeared in the pupil but did not rise appreciably above the pupillary plane. Instead it spread laterally towards the chamber angle. Fig. 1 (opposite) shows this phase. Later, the cream spread into the bulk of the aqueous, but a clear space, impermeable to the cream, was visible close to the cornea with the slit lamp (Fig. 2, opposite).

* Wilmot and Cassidy, Inc., New York.

FIG. 1.—Eye of *Strix aluco*, with cream spreading over the surface of the iris from the pupil.

This experiment again shows that the aqueous close to the iris is much more fluid than that close to the cornea.

It was then attempted to photograph small air-bubbles introduced into the anterior chamber by a needle through the limbus. It was difficult, however, to obtain good outlines of air-bubbles. Therefore small drops of fluorescent oil were injected instead, by means of an Agla micrometric syringe. The eye was placed in the plastic cuvette with the cornea facing up, the slit lamp was arranged vertically above it, and photographs were taken through the sides of the cuvette. The beam of light was carefully adjusted so as to pass through the vertex of the oil-drop. Fig. 3 shows a minute oil-drop in the mucinous layer covering the interior

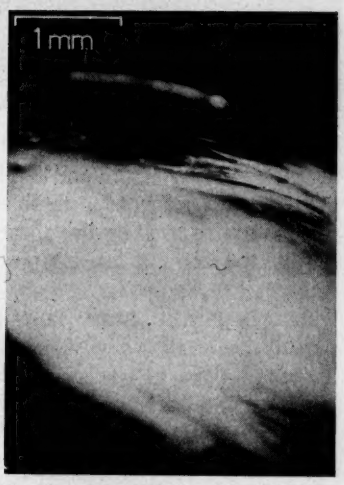

FIG. 2.—Eye of *Strix aluco*, showing how cream fails to mix with material beneath the cornea. Slit-lamp illumination, corneal section at top of picture.

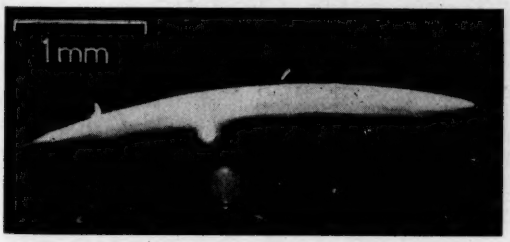

FIG. 3.—Eye of *Strix aluco*. Fluorescent oil-drop stuck in viscous material beneath cornea. Slit-lamp illumination, exposure 24 sec.

surface of the cornea. In one of these experiments minute air-bubbles were accidentally introduced together with the oil-drop. Fig. 4 shows them suspended in "mid-aqueous".

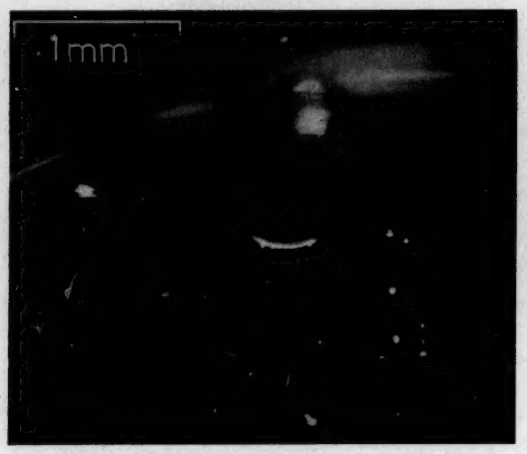

FIG. 4.—Eye of *Strix aluco*. Minute air-bubbles stuck in anterior chamber. Slit-lamp illumination, exposure 24 sec. Oil-drop and larger air-bubble visible close to cornea.

***In vitro* Observations on the Aqueous Humour of Owls.**—Removal of the aqueous humour from the living eye by suction through a needle can be very difficult. In order to avoid admixture of vitreous humour, pressure was always exerted on the cornea during the aspiration. None the less and despite the use of a very coarse needle, no flow was obtained in one bird; in this case the aqueous formed what was practically an elastic jelly, from which threads 30–40 cm. long could be pulled. A small part of this jelly rapidly liquefied when brought into contact with bacterial hyaluronidase. The rest of the jelly was dissolved in five times its volume of buffered saline containing a little diethyldithiocarbamate. The relative viscosity of this solution at 20°C. was 1·60 and it remained stable for hours. On addition of 6 V.R.U./ml. Hyason(R), the viscosity dropped to 1·08 in the course of one hour.

Discussion

We are able to confirm the statements of Abelsdorff and Wessely (1909). There is a mucinous substance in the aqueous of owls and it is most concentrated (or most highly polymerized) close to the cornea.

Our experiments indicate that the presence of mucin probably does not prevent the circulation of the aqueous, since the fluid close to the iris is much more mobile than that filling the anterior chamber. We have not obtained the impression, however, that there is a sharp boundary between a more mobile, central aqueous and a more viscous, peripheral one. Rather, the air-bubble and oil-drop experiments indicate a gradual transition. It would

have been of interest to see how the viscous material is arranged in the vicinity of the trabecular meshwork, but this we were not able to study.

As to the nature of the mucinous substance, our enzyme experiment, using a highly specific, bacterial hyaluronidase, indicates that hyaluronic acid or a closely-related mucopolysaccharide is a main constituent. The marked capacity for thread formation indicates that the molecular weight is very high.

The mucinous substance could either be deposited from the aqueous or formed by the corneal endothelium. Abelsdorff and Wessely observed that the second aqueous of owls is not slimy, and concluded that "the mucin, adherent to the posterior surface of the cornea, probably belongs more to this latter than to the aqueous". The gradient of viscosity observed in our experiments is also most easily explained if the mucin is produced by the endothelium and gradually dissolved (and/or depolymerized) by the circulating aqueous. The production of a hyaluronic-acid containing mucus by mesodermal endothelium is in no way unique, the synovial fluid being a well-known example.

As to the functional importance of the excessive amounts of mucin in the eyes of owls, one can only offer guesses. The anterior chamber of the owl's eye is relatively enormous (Fig. 5). If this volume had to be turned over at the same percentual rate as in other creatures, a very high rate of secretion of aqueous would be necessary. As it is, most of the aqueous is practically stagnant, and probably only the part in contact with the lens and iris is

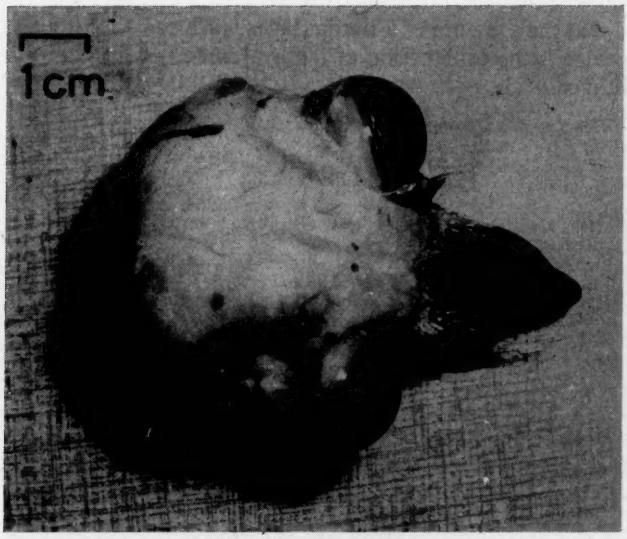

FIG. 5.—Head of *Strix aluco*, with skin removed, showing telescopic eyes.

rapidly exchanged. Thus a certain economy could be effected. Another possible function is to make the cornea self-sealing.

It is improbable that the mucinous layer covering the endothelium in the eyes of owls should have no counterpart in other creatures. We have therefore looked for a similar hyaluronidase-sensitive coating, albeit on a more modest scale, on the corneal endothelium of several animals and birds. As yet we have not been able to prove its existence to our own satisfaction. There is, however, a hyaluronidase-sensitive coating on the trabeculae of birds and mammals (Vrabec, 1957; Berggren and Vrabec, 1957); since the endothelial cells covering the trabeculae are closely related to the corneal endothelium, it seems possible that this coating is analogous to that of the cornea in owls and that it too is produced locally. Its existence probably explains the hyaluronidase-sensitivity of the resistance of the chamber angle (Bárány, 1957).

Summary

The corneal endothelium in the Tawny owl (*Strix aluco*), is covered by a thick layer of a mucinous substance which can be removed and studied *in vitro*. The substance is depolymerized by bacterial hyaluronidase and consequently contains hyaluronic acid or a closely related mucopolysaccharide.

The viscosity of the mucinous layer decreases with the distance from the cornea, and the aqueous immediately in front of the lens and iris is of low viscosity.

It is believed that the mucinous substance is produced by the endothelial cells, and that the presence of a similar layer produced by the endothelium of the trabeculae is the explanation of the hyaluronidase-sensitivity of the outflow resistance of the chamber angle.

This work was supported by the Swedish Medical Research Council.

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Brit. J. Ophthal. (1957) **41**, 31.

POSTERIOR CONICAL CORNEA*

BY

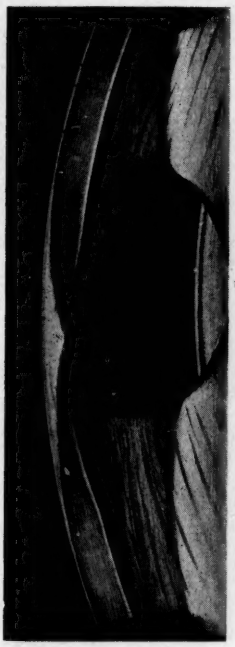
H. B. JACOBS

London

SINCE this condition was first described (Butler, 1930), only a handful of cases has been added to the literature. In view of its infrequency, some cases are presented and compared with previous descriptions.

Perhaps the name, although anatomically descriptive, is unfortunate, for it would imply that the condition has some relationship with the better-known conical cornea. In fact, there is no evident relationship beyond the unsubstantiated statement that the posterior form is a precursor of the ordinary form. The two conditions are so named merely because the cornea tends to become cone-shaped—throughout its thickness in ordinary keratoconus and solely in its posterior surface in keratoconus posticus. Two forms of the latter condition occur:

(A) Localized—keratoconus posticus circumscriptus.
(B) Generalized—keratoconus posticus totalis.



(A) Localized.—Seven cases have been recorded. Stallard (1930), Butler (1932), Goldsmith (1943), Leopold (1943), Wise (1944), Greene (1945), and Guimarães (1953) all describe a localized concavity of varying size in a part of the back of the cornea. Goldsmith's case (Fig. 1) is typical.

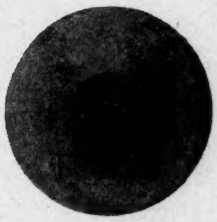


FIG. 1.—Case 5, slit-lamp appearance and sketch showing a typical posterior conus.

* Received for publication October 25, 1956.

Stallard (1930) makes no mention of a nebula in his patient but the other authors all comment on either a localized nebula or haze. The American authors (Leopold, 1943; Wise, 1944; and Greene, 1945) could obtain no history of trauma in any of their cases, and Leopold suggests that, since the condition has never been seen to develop after trauma, it is unjustifiable to assume that it is so caused. On the other hand, the case reported by Butler (1930) had a definite history of trauma, and there was reason to believe that in the case of Stallard's patient, a railway worker, the lesion was at any rate acquired. Six of the cases were men but Leopold's was a Negress. Five lesions were unilateral, one bilateral, one was in an only eye (Guimarães), and only one was associated with other possibly relevant ocular pathology. This (Greene's case) took the form of definite lens changes which were in line with the corneal lesion. Greene considered that, on the basis of the position of the lenticular opacities in the superficial layers of the foetal nucleus and their correspondence in position with the corneal lesion, the congenital origin of the latter could not be doubted.

Case Reports

Case 1, a woman aged 55, was admitted to hospital in June, 1953, for the removal of a cataract in the left eye. She had been observed in the out-patient department for 5 years and it had been noted that she had a corneal opacity in the left eye. On more detailed inspection, this was noticed to be associated with a posterior increase of curvature localized to that area (Fig. 2). This patient gave a history of trauma to the left eye in childhood. The right cornea was normal.

FIG. 2.—Case 1, slit-lamp appearance and painting of left cornea showing localized posterior conus and opacity situated in superficial layers of substantia propia.

Case 2, a woman aged 51, attended hospital in September, 1953, complaining of watering and blurring of the vision of the right eye for 5 days and blurring of the vision of the left eye for one day only.

On examination, some old pigment deposits were seen on the posterior corneal surface of the right eye, and a corneal opacity in the 8 o'clock meridian, deep to which was a localized posterior keratoconus. There were some cells in the anterior chamber. The left eye had acute glaucoma, presumably secondary to uveitis, and the patient was admitted to Moorfields Eye Hospital. During the course of investigation for the cause of the uveitis, the Wassermann reaction was found to be strongly positive.

The posterior conical cornea was localized in the situation described above. No similar lesion was present in the left eye.

Subsequently, a broad iridectomy was performed on the right eye for secondary glaucoma, and a sclerectomy on the left eye.

Case 3, a man aged 25, attended hospital complaining of discomfort in the right eye. A superficial corneal foreign body was removed and the cornea healed smoothly. In the course of routine examination, it was noted that this patient had a reduplicated lamina of lens opacity, white in the illumination of the slit lamp, and conjoined peripherally in the intermediate layers of the cortex. It was situated in the region of 6–7 o'clock and directly in front of it and a few millimetres from the limbus there was an unusual guttering of the posterior surface of the cornea (Fig. 3).

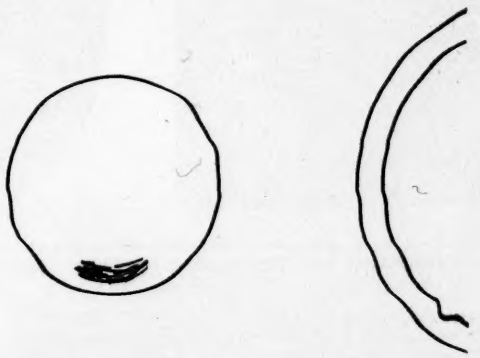


FIG. 3.—Case 3, diagram of unusual guttering of posterior surface of right cornea.

This was unlike other cases of posterior keratoconus described in this paper and elsewhere in that, instead of the lesion being oval or circular, it was merely a groove concentric with the corneal margin, approximately 5 mm. long and 1 mm. wide. This case is unusual in that it is the only one, other than that of Greene (1945), to show an associated congenital lenticular abnormality. Unfortunately no painting of this patient was done and only a diagram of the corneal condition can be presented.

Case 4, a short hunch-backed woman aged 55, attended hospital in July, 1952, with a 5-day history of pain and loss of vision in the right eye and also of vomiting. She had right acute glaucoma with a hypermature cataract. She was treated with eserine but after temporary improvement relapsed, so that an iridencleisis had to be performed. A few days later signs of infection developed, but these responded to intensive antibiotic therapy. 2 weeks after her discharge the eye was very red, with many keratic precipitates. Intensive treatment was advised but the patient failed to attend for a further 7 weeks when an enucleation was advised and duly performed.

In the course of clinical examination, the left cornea was noted to have three localized nebulae, and one of these showed a related posterior increase in curvature (Fig. 4). When the tension in the right eye first subsided a localized posterior conical cornea was seen similar in size and position to that in the left eye. There were no other opacities in the right cornea. A previous history of recurrent soreness of the left eye in childhood but no trouble with the right until the glaucomatous episode suggests that the two nebulae in the left eye not associated with the conus were the result of ulceration in childhood, but gives no clue as to the time of onset of the bilateral lesion. The previous history also suggests a certain lack of observation in the patient. Apart from the corneal condition, no other abnormality was seen in the left eye. The vision was 6/18 pt.

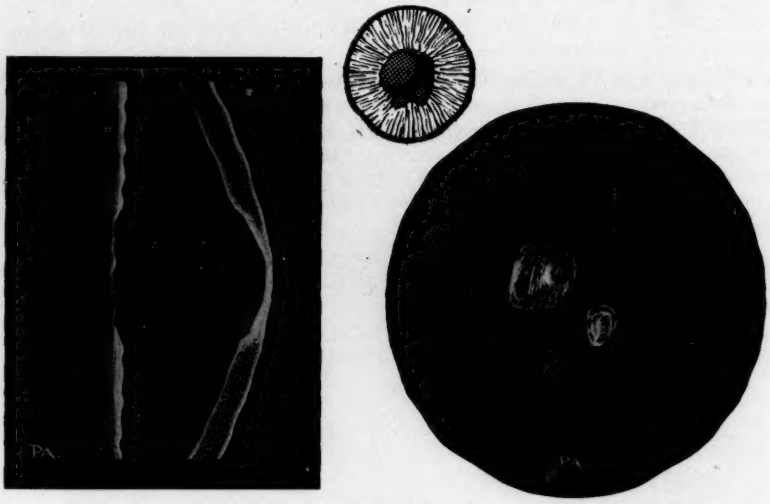


FIG. 4.—Case 4, left cornea showing localized posterior keratoconus posticus (depth of cone exaggerated and schematized). This lesion was related to the largest nebula, the others being the result of ulceration in childhood.

The enucleated right eye was sent for section, but the keratoconus posticus could not be demonstrated histologically. It is difficult to explain this, but possibly the depth of the posterior excavation was too slight to show, bearing in mind the unavoidable distortion that must occur in the preparation of histological sections. If and when a similar opportunity arises alternative techniques will be tried.

Case 5, a man now aged 70, is that recorded by Goldsmith in 1943 (Fig. 1). He was examined again by me in 1955. A description is appended for the sake of completeness.

He was first seen in January, 1942, with a foreign body in the left eye. He showed bilateral symmetrical lesions of keratoconus posticus circumscriptus. He has been seen at irregular intervals since, the last time being in November, 1955.

There appears to have been no alteration in the corneal condition but the refraction has changed.

January, 1942: Right eye +5·5 D sph. 6/9
Left eye +5·5 D sph. +1·00 D cyl., axis 95° 6/12

September, 1954: Right eye +6·00 D sph. +1·50 D cyl., axis 95° 6/9
Left eye +7·00 D sph. +1·00 D cyl., axis 95° 6/12

An intervening refraction in 1949 showed +1·00 D cyl. in the right eye.

The clinical appearance with a loupe and focal illumination was of a localized symmetrical nebula in each eye. Slit-lamp examination revealed a posterior concavity, an opacity of the superficial substantia propia, a Hudson's line below, and some Hassall Henle bodies in the endothelium and localized to the site of the lesion.

***Case 6, a girl aged 13,** gave a rather vague history of longstanding visual defect; her vision could be improved only to 6/18 in each eye with −6·00 D cyl. There was a nebula in each cornea, the lesion being larger in the left eye than the right; the slit lamp showed posterior conical corneae similar to the previous case but larger and more centrally placed.

Keratoscopy showed a marked distortion of the rings consistent with a regular corneal astigmatism, no localized defect being noted in the region of the conus defects.

This patient was fitted with contact lenses in Mr. Frederick Ridley's clinic; with them vision was improved to 6/12 in each eye.

Case 7, a man aged 55, attended hospital with bilateral cataracts, both of which were eventually extracted by Mr. Goldsmith. Faint, greyish, localized, eccentric corneal nebulae, bilaterally and not quite symmetrically placed, had been noted. Each nebula was related to a localized posterior concavity, the opacity being superficially placed in the substantia propia and showing some irregularly-disposed greenish pigmentation. Descemet's membrane in the region of the conus showed a slight brownish tinge. Corrected vision was 6/9 in each eye and no history relevant to the corneal lesions was elicited. The corneal appearance was similar to that in Case 5.

Case 8, a boy aged 15, had lived in Ireland until the age of 7. He attended school in England from that age till 15 and, during that time, had an eye test, but did not remember anything about it. On leaving school at 15 and applying for a job, his vision was found to be poor in both eyes, the left being worse than the right, so he sought hospital advice.

Questioning revealed that he had never been troubled subjectively and that he had no memory of any redness or discomfort in either eye.

The eyes were white and the visual acuity was 6/24 in the right eye and counting fingers at 1 foot uncorrected in the left. The right vision could be improved to 6/18 with −1 D cyl., axis 45°, and to 6/12 with a stenopoeic aperture. Retinoscopy on the left side indicated the need of −7·25 D sph., −3 D cyl., axis horizontal, but no significant improvement was obtained with such a lens and the eye was presumably amblyopic.

The right cornea showed a diffuse central haze and a denser opacity to one side. In relation to the former there was a posterior concavity and a Hudson's line, and the opacity was in the anterior part of the substantia propia. The endothelium was golden in colour. A brush of deep vessels ran to the denser opacity. The left cornea had many vessels in the deep substantia—all round—penetrating the cornea but avoiding a faint nebula in the central area. Related to this was a posterior corneal concavity; the opacity was in the middle part of the substantia propia.

The eyes were otherwise apparently healthy. The Wassermann reaction was negative.

Case 9, a man aged 49, was the father of Case 8. He had no ocular complaints and no history of any previous eye troubles. Vision in the right and left eyes was 6/12 and 6/9 respectively, and in the centre of each cornea a faint greyish nebula was visible. In the right eye, there was a related posterior concavity and an excess of Hassall Henle bodies, and in the left a mere posterior dimpling was related to the nebula. The endothelium on this side was of a golden hue. The opacity in both corneae was in the anterior part of the substantia propia.

The occurrence of these lesions in Case 9 suggested that the lesions in Case 8 might be hereditary rather than the result of previous attacks of interstitial keratitis.

** The author is indebted to Mr. A. J. B. Goldsmith for the description of this case.*

(B) Generalized.—Only three cases of keratoconus posticus totalis have been mentioned in the literature.

The first was described by Butler (1927), who stressed the following points:

(1) No nebula.
(2) No tears in Descemet's membrane.
(3) No increased number of corneal nerves.
(4) No Fleischer's ring.
(5) A perfectly regular, geometrically precise increase in curvature of the posterior surface of the cornea.
(6) Reflections of Placido's disc normal but elliptical.
(7) Structure of cornea normal but thinned.
(8) Sex female.
(9) Lesion unilateral.

In Butler's case the visual acuity was 6/18, and was only slightly improved by a cylinder of "plus 2, 3, or 4 dioptres at 45°".

In the discussion on Butler's case (shown at a meeting of the Ophthalmological Society of the United Kingdom in 1930) a further case was mentioned by Mr. P. L. Stallard.

A basin-shaped depression seen in the posterior surface of the cornea. This increase in concavity formed a perfect curve, involved one half of the cornea, and was fairly centrally situated. The spherical regularity of the anterior surface as evidenced by the keratometer mires and by the reflections of a Placido's disc was noted. No comment on the presence or absence of a nebula was made. The patient was a male Indian; the lesion was unilateral and thought possibly to be traumatic.

This case is probably better viewed as a keratoconus posticus circumscriptus; but is mentioned here because it was described as a companion case to that of Butler. (It is referred to in the preceding section.)

The second case (Ingram, 1936) showed a regularly increased curve of the posterior corneal surface similar to the case described by Butler.

Other points were as follows:

(1) A central haze was visible with a loupe.
(2) No Fleischer's ring.
(3) Some pigment deposits on the posterior corneal surface.
(4) Unilaterality.
(5) Sex female.

The visual acuity was less than 6/60 and unimprovable. No mention was made of the structure of the cornea, but presumably there must have been some change otherwise no haze would have been seen.

The third case (Ross, 1950) showed the following characteristics:

(1) Bilaterality.
(2) Sex female.
(3) Uniform increase of posterior corneal curvature. Anterior curvature was normal.
(4) Horizontal superficial Hudson's lines.
(5) Thinned but normal corneal stroma.
(6) Mixed astigmatism (right eye +3·25 D sph., − 4 D cyl., axis 108°; left eye +2·75 D sph., −4 D cyl., axis 72°), correction of which did not increase visual acuity which was 20/40 and 20/50 in the right and left eyes respectively.

Thus all three typical cases of this condition so far described in the literature were seen in women, who had had impaired vision for many years, and in all the condition was probably congenital. Ross remarks on the resemblance of the shape to the developing cornea.

Case Report

Case 10, a woman aged 49, presented with a history of poor vision in the right eye for as long as she could remember. She thought the condition was static but was unsure.

Examination.—Visual acuity was 1/60 in the right eye and 6/12 in the left unaided. The lids, conjunctivae, and ocular tension were normal.

The right cornea showed a faintly hazy appearance; the left cornea was clear apart from a small nebula near the limbus. The pupils reacted normally, the lens and vitreous in each eye were clear, the fundi showed no abnormality. The slit-lamp appearance of the right cornea showed marked thinning of the substantia propia associated with and apparently due to an increased curvature of the posterior corneal surface. The apex of the posterior "cone" and therefore the thinnest area of the cornea was just below and temporal to its centre (Fig. 5). The left cornea was normal.

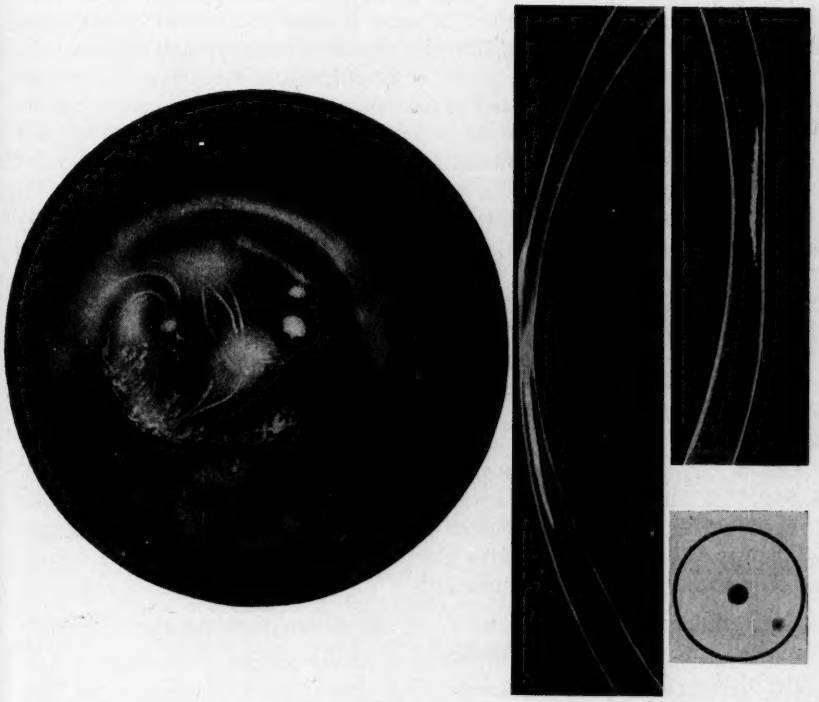


FIG. 5.—Case 10, keratoconus posticus totalis. View with a loupe and focal illumination to demonstrate the faint corneal haze and a ring of greenish pigmentation. Slit-lamp appearance showing thinning of cornea due to generalized increase in curvature of its posterior surface. Left cornea with a small incidental and unrelated nebula.

Placido's disc showed an irregularity just off centre towards 9 o'clock in the right eye. The reflections in the left eye were normal.

Retinoscopy gave the following refraction: right eye +1·75 D sph., −5·5 D cyl., axis 90°, but no improvement was effected either with these lenses or with a stenopoeic aperture. The visual acuity in the left eye was improved to 6/5 with +0·25 D sph., +0·75 D cyl., axis 180°.

Keratometry—The right eye was complicated by slight irregularity of the surface, but the readings were as follows:

$$\left.\begin{array}{l}\text{At } 15 \left\{\begin{matrix}7\cdot52\\7\cdot65\end{matrix}\right\}\text{mean } 7\cdot58\\ \text{At } 130 \left\{\begin{matrix}6\cdot55\\6\cdot79\end{matrix}\right\}\text{mean } 6\cdot72\end{array}\right\}\text{cylinder—}5\cdot5$$

In the left eye the readings were straightforward and corresponded with the refractive findings.

Discussion

(A) Keratoconus posticus circumscriptus.—Although little is known of the possible mechanism of formation of these corneal deformities, it is known that disturbances of Descemet's membrane and/or the corneal endothelium can give rise to opacities in the more anterior levels of the substantia propia. It would seem possible that such a disturbance in the very young could be accompanied either by a resorbtion of the deeper lamellae or failure in their formation, either of which might result in the formation of a localized posterior concavity.

The lesion of Descemet's membrane or the endothelium might take the form of a definite tear, some similar but subclinical loss of continuity, or merely a disorder of normal function of the endothelium in preserving the physiological status of the substantia propia.

This mechanism is consistent with prenatal or neonatal trauma or inflammation being responsible for the condition, while there are the additional possibilities that a failure in the normal development of either Descemet's membrane, the endothelium, or the substantia propia may be a causative factor.

Of the localized cases which constitute the first half of this paper, Cases 3, 4, 5, 6, 7, 8, and 9 are almost certainly congenital. Cases 1 and 2 could be congenital, but there is insufficient evidence to point one way or another. Of the five cases collected from the literature, three were probably of congenital origin and two possibly traumatic.

Cases 8 and 9 are of particular interest in that they represent the only instance so far recorded of a familial link in this condition.

(B) Keratoconus posticus totalis.—All these cases, including the one herein described, have a long history. All had had poor sight for as many years as they could remember. Ross's patient had fair vision, but it had not deteriorated at least during the previous 6 years. Harrison Butler stated

that he had watched two cases for 6 years and observed no change. All the cases failed to improve with correcting spectacle lenses; this makes it appear likely that all are amblyopic and argues for the congenital origin of the lesion.

None of the authors who have described these cases mentions a change in corneal structure, and Harrison Butler states that its absence is characteristic. The present case showed such a thinned appearance that it is difficult to make a point. All the authors comment on the regularity of the anterior surface.

The present case differs in small details from the generalizations made by Harrison Butler, but the other cases also show slight distinguishing features.

Ingram mentions a corneal haze and pigment deposits behind the cornea.

Ross noted a Hudson's line and a few Hassall Henle bodies peripherally. His is the only bilateral case on record.

In the present case, there was a definite faint haze, and the anterior corneal surface was slightly irregular as judged on the keratometer and with Placido's disc. No other author describes both these findings, and Harrison Butler states that in his case the reflections of the Placido's disc were regular.

All the cases were female.

No positive family history was given in the patients previously reported and none was obtained in the present case.

Only one of Harrison Butler's cases can be found in the literature though he gives the impression of having seen at least two. His generalizations would seem to exclude the present case from being grouped with the condition he originally described. However, there is certainly a general resemblance to his case and to the others referred to in the present report, and their many common features bear this out.

Summary

The literature concerning keratoconus posticus is reviewed. Some new cases are described. It is suggested that in nearly all cases the condition originates in early life and is probably present at birth.

It is a pleasure to record my debt to Mr. A. J. B. Goldsmith for his assistance in the preparation of this paper. For permission to publish their cases, I wish to record in addition my thanks to Mr. Ayoub, Mr. Gimblett, and Mr. A. Lister. Professor Sorsby kindly arranged for the keratometric readings.

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CASE NOTES

TRAUMATIC KERATOCONUS POSTICUS*

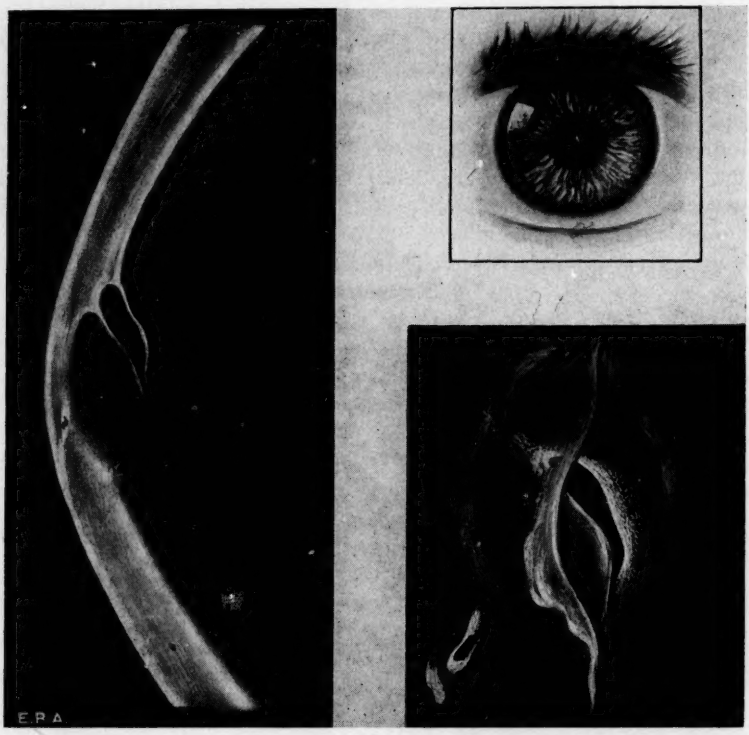
BY

H. B. JACOBS

London

Case Report

A man aged 46 attended the Royal Eye Hospital on June 13, 1956, complaining of floaters in front of the left eye. The left eye was normal on examination.



* Received for publication October 25, 1956.

There was, however, a history of an injury to the right eye at the age of 4 years, since when the vision had been impaired (visual acuity 6/36; 6/18 with pinhole). On examination two adjacent central corneal nebulae were seen, and behind the larger nebula the posterior corneal surface showed an increased concavity. The opacity was largely in the superficial part of the substantia propia. The torn ends of Descemet's membrane were curled and projecting behind into the anterior chamber.

This patient is reported as an interesting companion to the cases of keratoconus posticus described previously (Jacobs, 1957). The traumatic cause is undoubted in this instance.

The author is indebted to Mr. R. Pitts Crick for permission to publish this case and would like to express appreciation of the drawing done by Mr. E. R. Alexander of Stercks Martin Ltd.

REFERENCE

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CHOROIDAL SARCOMA WITH METASTASIS IN THE OPPOSITE ORBIT*

BY

J. FOSTER, W. HENDERSON, J. W. COWIE AND D. S. F. HARRIMAN

United Leeds Hospitals

THE DETAILS of this case are submitted for publication partly because of its rarity, only one similar case having been found in the literature (Philps and Ashton, 1949), and partly because of certain interesting details in the diagnosis and treatment. The patient described by Philps and Ashton, a woman aged 59 years, developed 2D hypermetropia, exophthalmos, and a palpable tumour in the left orbit 10 years after excision of the right eye for a choroidal melanoma. A tumour was removed from the muscle cone by a lateral orbitotomy, and 6 months later the loss of central vision, hypermetropia, and exophthalmos had been cured. Comparison of the sections of the orbital tumour with that of the choroid left little doubt that the second tumour was a metastasis from the first. Our own case is strikingly similar.

Case Report

A woman aged 56 had her right eye excised in 1951 (by Mr. F. Gamm in the Huddersfield Infirmary) for melanoma of the choroid; 4 years later, in October, 1955, the vision in the left eye began to fail rapidly with simultaneous development of exophthalmos, and she was referred by Mr. Gamm to the Leeds Infirmary for a contrast-medium *x*-ray of the orbit by the technique of Groves and Cowie (1955).

Examination.—In December, 1955, she had 4 mm. of exophthalmos (Fig. 1), papilloedema, a hemianopic scotoma to the outer side of fixation (to white objects of 3/2000

FIG. 1.—4-mm. left exophthalmos measured by Mutch's proptometer.

* Received for publication June 26, 1956.

and 15/2000), and marked limitation of eye movement up and in (Fig. 2).

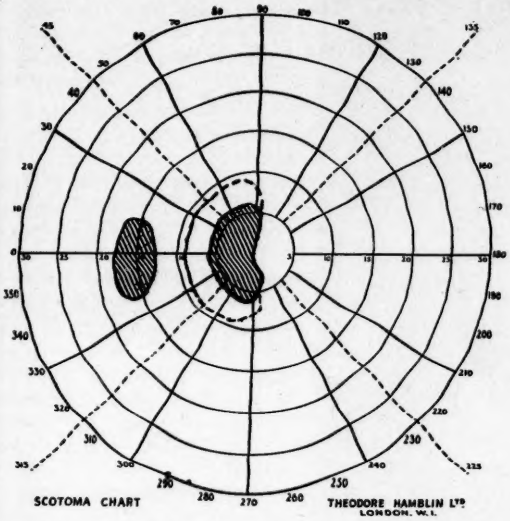

FIG. 2.—Scotomata 3/2000 and 15/2000 left eye, on December 15, 1955.

The visual acuity with +2 D sph./ +0·25 D cyl., 100° was 6/24, add +2·25 = N.10. A week later the scotoma had extended (Fig. 3) and the refraction with +3·5 D cyl. was 6/36.

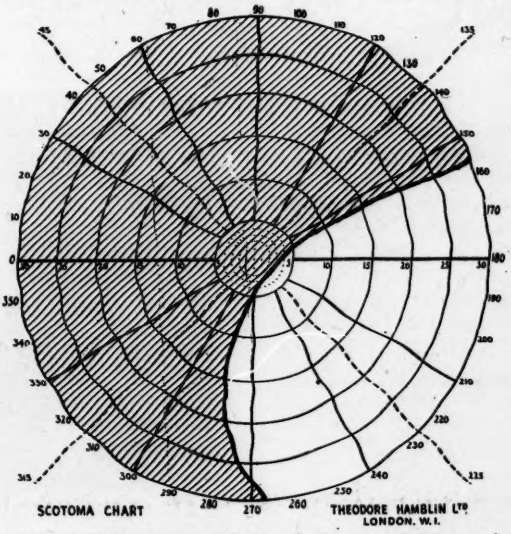

FIG. 3.—Scotomata 15/2000 left eye, on December 22, 1955.

Diodone X-Ray (*J. W. Cowie*).—*3·5 ml. 17·5 per cent. Diodone in 2 per cent. Novocain* was injected into the muscle cone and routine films were taken.

The appearances were rather unusual, as there was no true clover shape representing the muscle cone in the antero-posterior view, but a hollow, slightly irregular, circular opacity (Fig. 4, overleaf).

On the lateral view a "shelf" was discerned medium above and below the site of a normal muscle cone (Fig. 5, overleaf).

The appearances were those of a large mass in the muscle cone and mainly, if not entirely, confined by it.

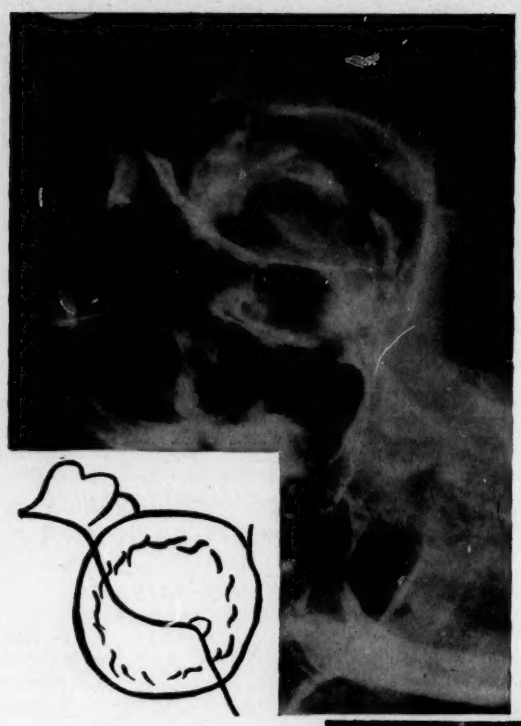

FIG. 4.—Diodone *x*-ray, antero-posterior view, showing a hollow, slightly irregular, circular opacity.

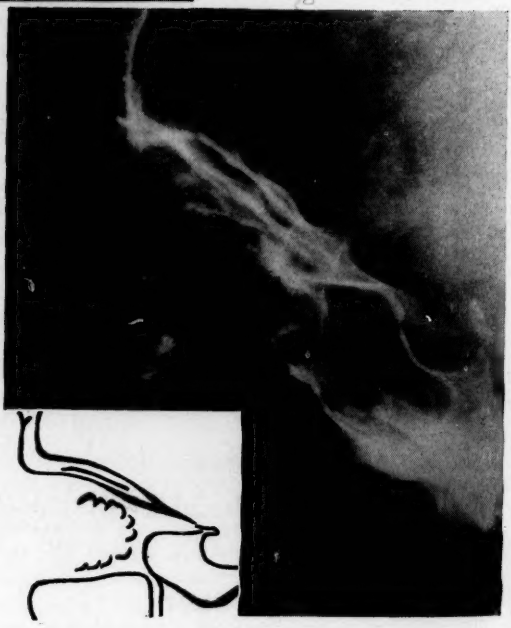

FIG. 5.—Diodone *x*-ray, lateral view, showing a shelf medium above and below the normal muscle cone.

Diagnosis.—At this time it was thought that there might be a metastasis from the excised eye in the orbit, or a growth arising from the left optic nerve sheath. As the hemianopic scotoma was located to the outer side of fixation, it was felt that the growth was probably located on the inner side of the nerve and that a transfrontal exploration was indicated.

The patient was referred to Mr. W. R. Henderson, who expressed the opinion that an exploration would only be justified if the patient were willing to run the risk of damage to the optic nerve during the operation, which would produce immediate total blindness. Since loss of the vision and ultimate loss of the eye would certainly occur in time, and the patient had already developed another mm. of exophthalmos, consent was given.

Operation (Mr. W. R. Henderson).—This was performed on February 6, 1956. A left transfrontal bone flap was made. The dura was stripped back to the sphenoidal ridge, and the orbital roof was removed from the frontal sinus back to the sphenoidal fissure. Retraction of the superior muscles laterally and of the trochlear nerve and muscles medially revealed a rounded tumour medial to the optic nerve which was displaced laterally but not invaded by the tumour. At first sight the tumour looked like a very ripe cherry but it was later found to be considerably larger, the size of a walnut, as it extended down to the orbital floor. It had a thin smooth capsule which at first dissected easily from orbital structures but deeper down there was no line of separation. The capsule was opened and a dark red, soft, solid tumour containing small blackish areas was scooped out. As the remaining capsule was firmly adherent and could not be removed without damaging normal structures the operation was terminated.

Pathology (Dr. D. S. F. Harriman, Leeds Infirmary Neuro-surgical Department).—After fixation in Bouin's fluid, the tissues were embedded in paraffin and stained by haematoxylin and eosin, Holme's silver method, and Fontana's method for melanin granules.

The tumour proper consisted mainly of fairly closely packed plump spindle cells arranged in interlacing bundles. The nuclei were plump, oval, and sometimes indented. There was a distinct nucleolus, and often a central nuclear fold running in the long axis of the nucleus. Mitotic figures were scanty. The cytoplasm was finely granular, and the cytoplasmic membrane poorly defined. Numerous thin-walled vessels were present throughout, and sometimes the cells were orientated at right angles to them. In a few areas only, melanin was found in the cytoplasm, generally as a cluster of coarse granules. Although the main pattern of the cells was of the spindle cell variety, some areas were found where the cells were polygonal, with clear cytoplasm, and arranged into alveoli by delicate connective tissue strands. No nerve fibres were found within the tumour.

The capsule consisted of uncompressed fibro-fatty tissue containing muscle fibres, and was invaded by small islands of tumour cells.

This is obviously a melanoma. Histology will not reveal whether it is primary or secondary at this site.

Progress.—The operation was followed by marked oedema and ptosis of the upper lid, but on February 18 it was possible to open the eye, and the exophthalmos was decreasing. Although movement upward and inward was still limited, the visual acuity with +3 D sph. was 6/9, add +2·25 = N.6. The visual field had also begun to improve (Fig. 6, overleaf). Six months later, on June 15, the patient could read N.5 print and the exophthalmos and papilloedema had disappeared. No campimetric study was made on this occasion.

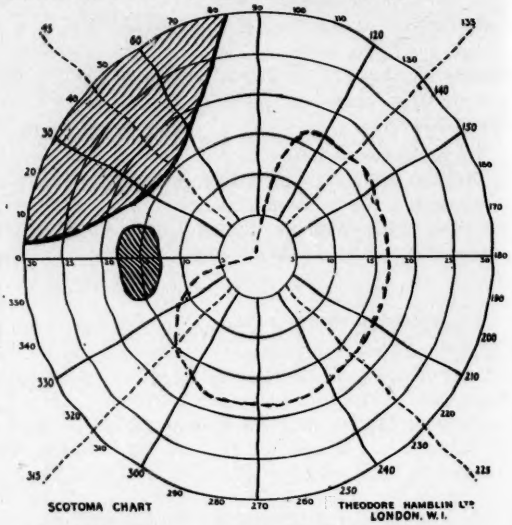

FIG. 6.—Scotomata 5/2000–15/2000 red field, left eye, on February 16, 1956, 10 days after operation.

Discussion

Slides of the orbital growth were submitted to Dr. Norman Ashton at the Institute of Ophthalmology. Fig. 7 shows the original melanoma of the choroid.

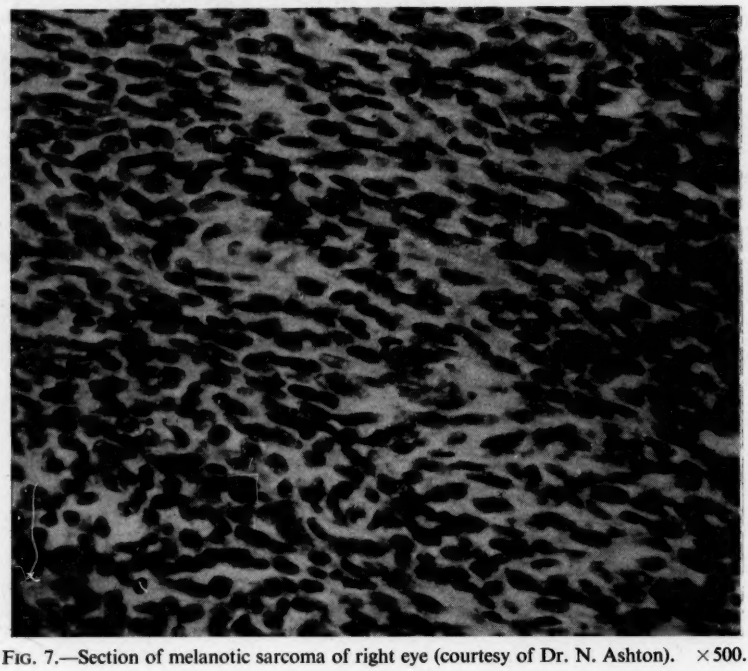

FIG. 7.—Section of melanotic sarcoma of right eye (courtesy of Dr. N. Ashton). ×500.

Fig. 8 shows the orbital growth.

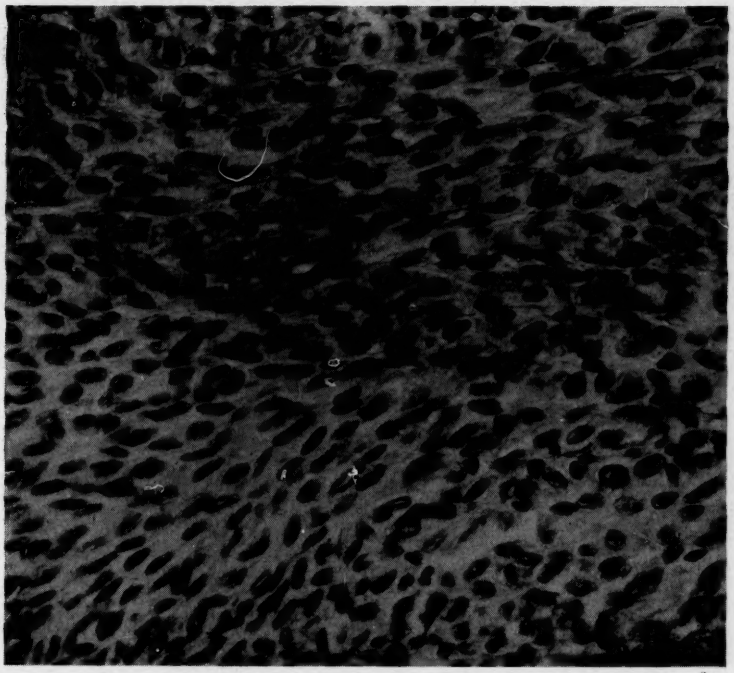

FIG. 8.—Section of orbital tumour (courtesy of Dr. N. Ashton). ×500.

We are most grateful to Dr. Ashton for the following comment:

I have examined the slides of the original intra-ocular growth together with the slides of the orbital tumour. There is no doubt that the histology is identical, both showing a malignant spindle-celled melanoma, so that it would appear fairly certain that the tumour of the left orbit was a delayed metastasis from the right eye.

Summary

A rare case of metastasis of the contralateral orbit from a choroidal melanotic sarcoma is described. Transfrontal exploration was indicated by a hemianopic scotoma (which suggested a tumour was pressing on the inner side of the nerve) and localization by Diodone. Subtotal removal of the tumour had restored vision to normal 6 months later, but in September, 1956, the family doctor reported that the liver was enlarged and that the exophthalmos had recurred.

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Brit. J. Ophthal. (1957) **41**, 48.

NEUROBLASTOMA*

BY

W. J. LEVY

Moorfields Branch, Moorfields Westminster and Central Eye Hospital, London

A SURVEY of the literature reveals that about five hundred cases of neuroblastoma have been recorded (Pack, Horning, and Ariel, 1952; Ingalls, 1953; Phillips, 1953).

The commonest site of origin is the suprarenal region, followed by the retroperitoneal area; occasionally other abdominal sites and the mediastinum are incriminated, and many cases do not allow of an anatomical diagnosis of origin (Phillips, 1953). Of all the cases described by these authors only five of 81 reported by Phillips are recorded as arising primarily in the orbit. Phillips remarks that clinical evidence of an orbital primary may be very misleading. No mention of a *post-mortem* examination is made, and it is presumed that a clinical diagnosis alone is offered. Authors who identify retinoblastoma with neuroblastoma and so claim orbital primaries in their cases, have been ignored in this review. The case now reported thus has unusual interest.

Case Report

A boy aged 3 years and 3 months was admitted on October 11, 1955; 4 months previously he had bumped the right side of his forehead, and a month later had been found to have a severe nasal infection (with discharge of mucopus from the right nostril) associated with severe right frontal headache. These symptoms were immediately followed by an acute proptosis of the right eye. His family doctor treated him with two short courses of oral chloramphenicol, which resulted in remission of his condition. In mid-August the right proptosis recurred and on September 30, 1955, a diffuse swelling was noted in the right temporal fossa. An *x*-ray report accompanied the child when he was referred for a further opinion and treatment; this indicated there to be decalcification or erosion of the sphenoidal ridge. The mother, who appeared to be an accurate witness, stated that the boy had had an extensive birthmark across his chest and on his right upper lid and that these had regressed until all that remained was a faint stain on the right shoulder.

Examination.—He was a well-nourished child. Apart from the skull, orbital, and shoulder lesions no abnormality was discovered. A gross, irreducible, non-tender proptosis with infero-temporal displacement of the right eye was obvious (Fig. 1, opposite).

The tip of a cyst-like mass was palpable through the upper lid under the superior orbital margin and was easily displaced back into the orbit. No bruit was heard, although breath sounds were exaggerated over the right frontal bone. An indefinite soft swelling was discernible in the right temporal fossa, but no fluctuation could be transmitted hence to the orbital mass. Ocular movements were not at all restricted. Slight oedema of the

* Received for publication, September 20, 1956.

FIG. 1.—Proptosis of right eye. The diffuse swelling in the temporal fossa is just discernible in this photograph. The recent wound on the upper lid is the site of the biopsy.

lids was present, but there were no ecchymoses and the eye was white. Corneal sensation was diminished and there was some degree of papilloedema. All other ocular findings were normal, as were the blood reports.

Diagnosis.—Probably sarcoma of the orbit.

Radiologist's Report (Dr. M. Lederman; October 24, 1955).—Definite areas of bony destruction of the right orbit which is larger than the left—suggestive of neoplasm.

Biopsy (October 27, 1955).—At operation a large, smooth-walled cystic mass, bluish in colour, with a tough outer coat, was found in the superolateral region of the right orbit, disappearing back into the depths. The cyst contained a little bloodstained fluid.

Biopsy (November 3, 1955).—Section shows two small pieces of fibrous tissue invaded by masses of round cells, with hyperchromatic nuclei arranged in dense clumps containing small aggregations of cells; one or two of these resemble rosettes. The histological picture suggests a round cell sarcoma, leukaemic deposit or neuroblastomatous and the latter seems the most likely.

High-Voltage Therapy (November 8 and 16, 1955).—3120r, KV 220, was given to the anterior and lateral aspects of the right orbit.

Radiological Examination.—Chest and intravenous pyelograms showed nothing abnormal.

Progress.—Although the child was pale and tired by this time, his condition remained fairly good. Proptosis now was 3 to 5 mm. On January 13, 1956, his general condition had deteriorated and a spinal lesion was suspected. Radiography showed collapse of the dorsal and lumbar vertebrae. High voltage therapy (1100r and 600r) was given to the dorsal and lumbar spine over 16 days. On January 21, 1956, deterioration of his general condition continued and a blood transfusion was given.

By March 9, 1956, he was very wasted and anaemic. No proptosis remained nor any temporal fossa swelling; the eye was white and the fundus normal; ocular movements were in no way restricted. There was no paraplegia but he had considerable pain in his limbs. Sphincter control was unimpaired.

The child died on April 10, 1956.

Post-mortem Report (Dr. D. A. L. Bowen).—The orbital plate of the right frontal bone appeared normal, but posteriorly the greater wing of the sphenoid and the adjacent

pituitary fossa were reddish in colour and softer than normal. This extended to the margin of the temporal bone laterally and to the cavernous sinus medially. On removal of the orbital plate of the frontal bone, a soft oedematous mass of brownish tissue was seen (Fig. 2) which lay above and could not be separated from the superior rectus muscle. It also lay above and to the right of the optic nerve. This mass was thought to be the primary tumour. There was no attachment to the optic nerve itself and the nerve was cut across at the entry to the globe. The brain and spinal cord showed no abnormality

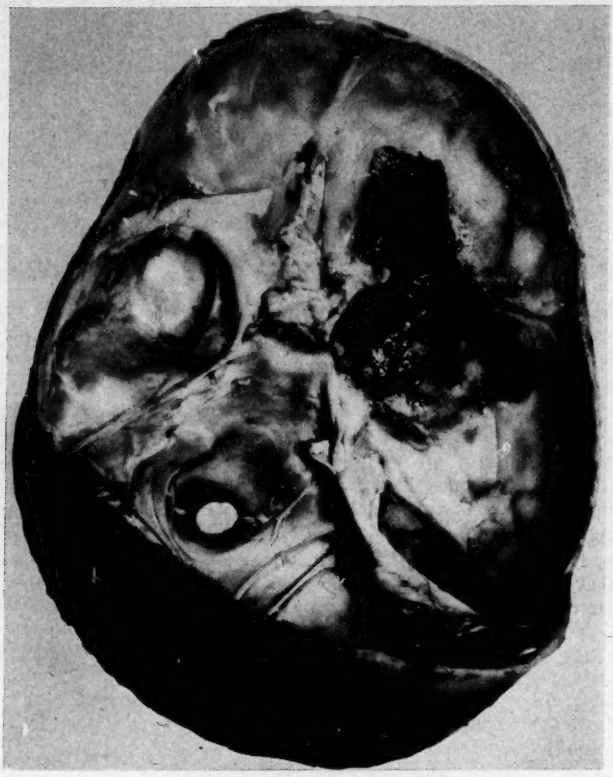

FIG. 2.—*Post-mortem* photograph showing the soft tumour mass exposed by removal of the superior orbital plate, sphenoidal ridge, and lateral wall of the pituitary fossa, in the basal aspect of the skull, viewed from above.

No tumour was seen in the region of the cervical sympathetic ganglia. The lungs manifested some reddish areas but were otherwise normal.

The peritoneal cavity and the entire gastro-intestinal tract were normal, as were the liver, spleen, gallbladder, and their surrounding areas. No evidence of tumour was found in the adrenals, and the coeliac plexus and the sites of the other abdominal ganglia appeared normal. The mediastinal and abdominal lymph nodes and surrounding areas were normal.

The T.12, L.1, and L.3 vertebrae were collapsed, abnormally red in colour, and softer than the surrounding vertebrae.

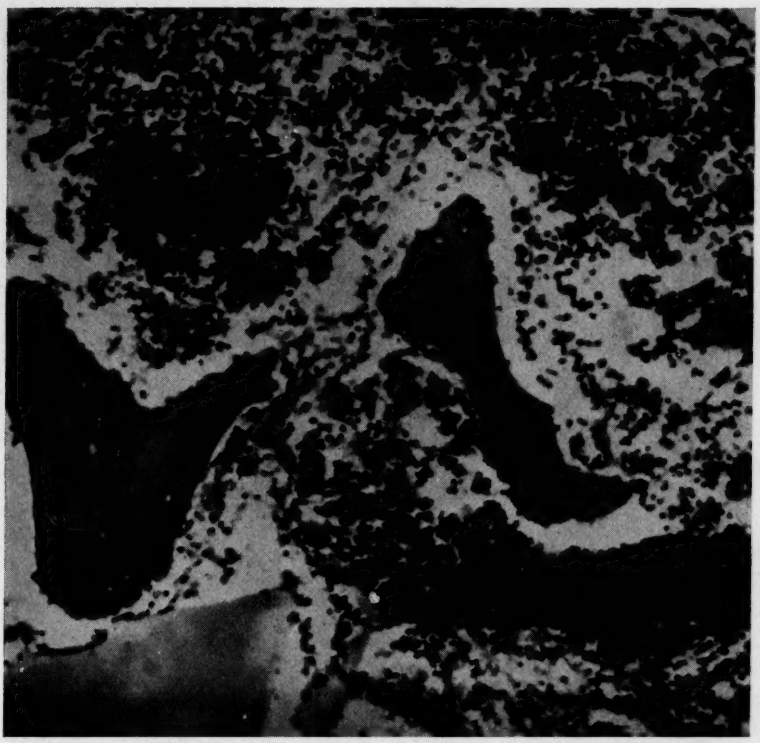

FIG. 3.—Photomicrograph (× 200) of section of lumbar vertebra showing replacement of bone by tumour cells in an area of intense infiltration. A few rosettes are to be seen.

Histology.—Tumour tissue was present in the lungs, spleen, liver, pituitary fossa, sphenoid bone, and vertebrae (Fig. 3). The individual cells were small, resembling lymphocytes in appearance, with very scanty eosinophilic cytoplasm, almost the entire cell being occupied by a darkly-staining spherical nucleus having a tendency to be irregular in shape and size. In one vertebral metastasis many cells showed a tendency to form rosettes. One definite rosette was identified (Fig. 4, overleaf), confirming the diagnosis of neuroblastoma. Sections from each lobe of the lungs showed alveoli outlined by tumour cells lying in the alveolar capillaries. In the liver, columns of neuroblastoma cells were present between the liver cells. The splenic pulp contained similar cells. The retro-orbital mass was composed of rather acellular fibrous tissue, showing numbers of pigment-containing macrophages, but no tumour. Both suprarenal glands and coeliac ganglia were normal.

Cause of Death.—Orbital neuroblastoma with spread to sphenoid bone and pituitary fossa, and metastasis in lungs, liver, spleen, and vertebrae.

Discussion

The history and necropsy findings suggest that this neuroblastoma arose in a retro-orbital ganglion. After radiotherapy the orbital portion was

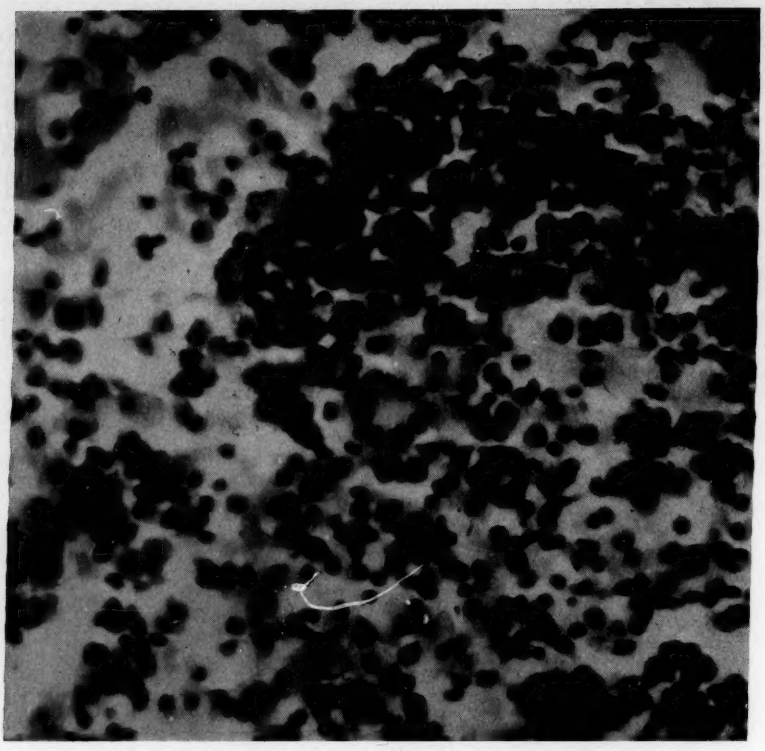

FIG. 4.—Photomicrograph (× 680), higher magnification of Fig. 3, a rosette excellently demonstrated (centre).

destroyed, but haematogenous dissemination had occurred, causing heavy deposits in the liver, lungs, and vertebrae. Despite careful search, no evidence was found of any tumour arising in other possible sites in the thoracic or abdominal ganglia.

An extremely difficult exercise in diagnosis was offered by this case, because of the history of the commencing infection, which followed on trauma, regressing angiomatous skin lesions involving the eye affected, and an orbital lesion with no ecchymosis or limitation of movement and with no other discoverable lesions. On reflection, one investigation might have helped in the early stages, *viz.* a sternal marrow puncture to reveal haematogenous spread of the tumour.

Summary

The first case of neuroblastoma arising primarily in the orbit, with a clinical report and necropsy findings, is recorded.

I wish to thank Mr. R. C. Davenport and Mr. E. Perkins in whose care this patient was, for permission to report this case; Dr. N. Ashton and the Pathology Department of the Institute of Ophthalmology for the biopsy report and assistance in the preparation of specimens for illustration and the Medical Illustration Department for these pictures; Dr. M. Lederman and the Radiotherapy Department of the Royal Marsden Hospital for their co-operation in the treatment of this patient and their assistance in producing records, radiographs, and photographs; and Dr. D. A. L. Bowen of the Pathology Department of the Royal Marsden Hospital for his *post-mortem* report.

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Brit. J. Ophthal. (1957) **41**, 54.

RETINITIS PIGMENTOSA AND GAUCHER'S DISEASE*

BY

A. D. CHARTERS

Nairobi, Kenya

Case Report

A man aged 38, of Jewish descent, spent his early life in Germany, and came to live in Kenya in 1939.

Family History.—There is no history of Gaucher's disease in his family. His mother is alive and well. His father died of cancer of the kidney. He had no brothers or sisters. He was not married.

Past History.—He had measles as a child, and had occasionally suffered from malaria, the last attack occurring in 1950; he stated that it took him much longer than the average person to recover from an attack, which usually lasted about a fortnight.

As a baby of about one year he had developed recurrent attacks of pyrexia. His spleen was found to be enlarged, and steadily increased in size. There was no history of jaundice. In 1926, at the age of 12, a diagnosis of Gaucher's disease was made and splenectomy was performed; 2 years later a secondary accessory spleen was said to have been found and also removed. He then believed and felt that he was cured, though his liver steadily increased in size. His only abdominal complaint was one of fullness after meals. He had no other digestive disorder, and did not suffer from nausea or vomiting. His bowels were regular, and he had a very good appetite, though he was thin and did not put on weight. He complained that his liver was painful if knocked. He had no dyspnoea or cough. His stools and urine had always remained of normal colour. After July, 1952, he occasionally woke up with a little blood in his mouth.

The first sign of ocular disease was noticed in 1936, at the age of 22, when he noticed difficulty in seeing at night, but an ophthalmological examination at the Zürich Eye Infirmary revealed no abnormality. After his arrival in Kenya in 1939, his sight steadily deteriorated; his night-blindness became progressively worse and he discovered that he was unable to read a luminous watch at night; he became unable to drive a car at night, and by 1952 was unable to drive even by day. In 1951 he found that the periphery of his field of vision was becoming defective, as exemplified by inability to see a car coming out of a side road when he was driving. During 1951 he found it a strain to read even in a good light. The sight of his left eye had always been worse than that of his right eye.

He rarely drank any alcohol and his smoking averaged 4 to 10 cigarettes a day.

Examination (*July* 16, 1952).—The patient was well built, height 5 ft. 4 in., pulse 78, blood pressure 120/70. He had a rather dark pigmented skin. No enlargement of his lymphatic glands could be detected. There was no pallor of the conjunctivae. The mouth and throat were healthy. No abnormality was found in heart, lungs, or nervous system.

The liver was extremely enlarged, the lower edge being palpable two finger-breadths below the level of the umbilicus on the right side and three finger-breadths below the costal margin on the left side.

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Ophthalmological Report (*Dr. K. Simon*).—In 1945 the vision in the right eye, with a small astigmatic correction, was 6/9, and that in the left eye 6/12. No other abnormality was detected. No change was seen 2 years later. On July 9, 1952, a marked deterioration was observed:

"Both fundi show pigment spots of the bone corpuscle type mainly in the periphery. Left fundus more affected than the right. Left disc pale and of a waxy appearance, blood-vessels thin. The fundi have the characteristic signs of retinitis pigmentosa. Vision in the right eye 6/18 and in the left eye 6/60. The visual fields show a ring scotoma with a small central field defect. In a reduced light this field is even smaller than in normal light." (Figure.)

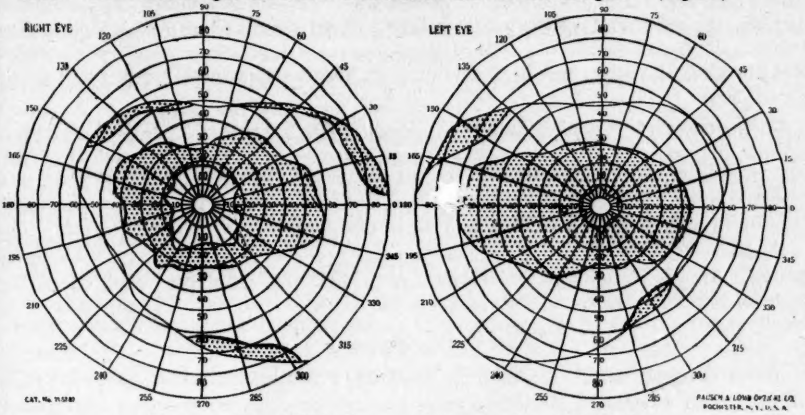

FIGURE.—Visual fields 10 mm. white target in artificial light.
Right eye July 6, 1952. Left eye July 5, 1952.

Radiologist's Report.—An *x*-ray examination after a barium meal in 1942 is said to have revealed no abnormality except adhesion of the stomach at the site of the old splenectomy operation and straightening out of the duodenum.

An *x*-ray of the chest by (Dr. W. G. S. Hopkirk) in July, 1952, revealed no abnormality, but the right and left lobes of the liver appeared greatly enlarged, and showed uniform opacity. No splenic shadow could be differentiated. The spine and ribs appeared normal. No recognizable lipoidotic changes were seen in the limbs examined.

Laboratory Investigations.—A fractional test meal in 1924 was within normal limits.

Blood Count (July 11, 1952): red cells 4,200,000 per c.mm., haemoglobin 95 per cent., leucocytes 12,800 per c.mm. Differential count: neutrophils 54 per cent., lymphocytes 45 per cent., basophils 1 per cent., one normoblast seen, cells otherwise normal; no poikilocytosis or anisocytosis.

Marrow Biopsy (July 25, 1952): polymorphs, band forms, and metamyelocytes 45 per cent., lymphocytes 35 per cent., eosinophils 1 per cent., myelocytes 9 per cent., normoblasts, various types, 10 per cent. Smudge cells 11 per 100 cells. No Gaucher cells seen. M/E ratio 5·5. Examination of smears from haemolysed deposit showed no Gaucher cells (the late Brig. R. P. Cormack).

Blood Cholesterol (July 11, 1952): 135 mg. per cent.

Serum Protein: total protein 6·8 gm. per cent., albumin 3·6 gm. per cent., globulin 3·2 gm. per cent., A/G ratio 1:1·1.

Thymol Turbidity: 9 units.

Serum Colloidal Gold: quantitative 554100, qualitative positive.

Kahn Test: negative.

Platelet Count: 452,000 per c.mm., prothrombin level 80 per cent. of normal, coagulation time 3·5 min., bleeding time 3·5 min.

Serum Vitamin A Estimation (Mr. A. W. Pearson): Vitamin A determined by the colorimetric method (Dann and Evelyn, 1938): corrected for carotenoids 105·5 international units per 100 ml.

A section of the spleen removed in 1926 had been preserved and was examined in January, 1953, by Dr. G. L. Timms who confirmed the diagnosis of Gaucher's disease.

Treatment.—Fifteen intramuscular injections, each of 100,000 units Crooke's vitamin A, were given daily for 9 consecutive days, followed by one injection twice a week. The injections were followed by a course of Crooke's vitamin A capsules of 33,000 units, one capsule three times a day.

Progress.—In November, 1952, 3 months after the commencement of vitamin A therapy, the patient thought that there was a slight improvement in his sight. For example, he found that he was able to see a clock in a dark corner of his room, which was previously invisible, and he also noticed an improvement in his reading and in his visual field.

Ophthalmological Examination (*Dr. K. Simon*).—On December 3, 1952, there was a definite improvement in the patient's eyes. The visual acuity of the right eye had improved from 6/18 to 6/12, (that of the left eye, which had always been very poor, was 6/60 and could not be properly recovered owing to considerable amblyopia). The visual field of the right eye had increased by 5° in all directions.

Result.—The patient discontinued the vitamin A capsules in March, 1953, owing to nausea. He died in June, 1956, at the age of 42, from a fractured skull caused by walking into a moving lorry, presumably as the result of his defective visual field.

Discussion

According to Cogan (1950), "the prime pathological changes in retinitis pigmentosa consist in a disappearance of the rods and cones and outer nuclear layer. The inner retinal layers are characteristically preserved, even later in the disease. The pigmentation of the retina is a secondary process, probably conditioned by having the sievelike external lining membrane in contact with the pigment epithelium with subsequent migration of epithelial cells into the retina."

Nicholls (1949) stated that "the cause of retinitis pigmentosa is unknown". Biró (1948) considered that the vascular spasm observed by himself and by Redslob (1947) as an antecedent to retinitis pigmentosa, probably resulted from posterior pituitary hormone (Vasopressin), whereas Verhoeff (1931) believed that the circulatory changes were secondary to the retinal atrophy.

The association of retinitis pigmentosa and Gaucher's disease in the case described above may be a pure coincidence, but the absence of any family history, or of any evidence of subjective or objective eye signs at an early age, favour an acquired cause. It is therefore relevant to consider the features common to the two diseases.

(*1*) *Abnormalities of Lipoid or Cholesterol Metabolism.*—Gaucher's disease is "thought to be a constitutional disturbance of lipoid metabolism" (Whitby and Britton, 1950). Levy-Wolff (1940) claimed that there was a connexion between retinitis pigmentosa and cholesterin metabolism, finding figures of blood cholesterin at the upper limit of normal (180 to 200 mg. per cent.) in very recent cases, "whereas all of the advanced cases showed increases occasionally up to astonishingly high proportions from 360 to 380 mg. per cent."

(*2*) *Pigmentation.*—Both diseases are associated with increased pigmentation, which has a predilection for the skin and sclera in Gaucher's disease and for the retina in retinitis pigmentosa. The discovery of a melanophore-stimulating hormone in the urine in cases of retinitis pigmentosa has been cited in favour of the theory of a pituitary origin for this disease (Nicholls, 1949), an argument which receives further support from the occasional association of the disease with the Laurence-Moon-Biedl syndrome.

(*3*) *Hepatic Disease.*—The case described above showed not only gross hepatic enlargement, but also defective liver function. According to Duke-Elder (1940), hepatic disease has frequently been associated with pigmentary degeneration of the retina, owing to the known association between diseases of the liver and a deficiency in the regeneration of visual purple and night-blindness. A clinical association between cirrhotic and chronic inflammatory conditions of the liver and degeneration of the pigmentary epithelium of the retina was reported by Baas 1894), Hori (1895), Purtscher (1900), and Koyanagi (1920), but although it has been recorded that the subjects of pigmentary degeneration do suffer from hepatic dysfunction (Takahashi, 1925) this association appears to be by no means invariable.

(*4*) *Vitamin A Metabolism.*—Pillat (1929) reported pigmentation of the conjunctiva resulting from vitamin A deficiency. Levine (1933) considered that retinitis pigmentosa might be caused by lack of vitamin A, but he obtained disappointing results from the administration of large doses of cod-liver oil to his patients, possibly, as he suggests, through the inability of the diseased retina to utilize the vitamin A supplied. Fuchs (1951) described a bilateral disease of the retina, similar to retinitis pigmentosa albescens, which results from vitamin A deficiency and which is cured by vitamin A therapy; retinitis pigmentosa albescens has a relationship to retinitis pigmentosa, the two conditions sometimes coexisting in the same family, hereditary factors being sometimes present, and the characteristic appearance of retinitis pigmentosa albescens having been observed to change to those of retinitis pigmentosa (Carroll, 1950).

According to Cogan (1950), the similarity of the changes observed in chronic experimental avitaminosis "A" and those of retinitis pigmentosa are so striking as to merit consideration:

> "These changes, as observed in rats and dogs, consist in degeneration of the rods and cones and of the outer nuclear layer of the retina with preservation of the bipolar cell layers. In other words, chronic avitaminosis "A", which is known to produce the same functional abnormality as is found in retinitis pigmentosa, produces the same histological changes in the retina. . . . It is by no means excluded that the fundamental abnormality is a metabolic one in which the degeneration of the retinal elements is secondary. It is not impossible, for instance, that the prime abnormality is in a local inability to utilize the vitamin A supplied to the pigment epithelium. It would seem reasonable at the present time to suppose that owing to some defect in the enzyme system, the rods and cones or the pigment epithelium were unable to utilize the vitamin A supplied to them. Such a hypothesis seems the most reasonable explanation for the similarity of the pathological changes in retinitis pigmentosa of human beings to those of chronic vitamin A deficiency in animals."

As Leitner (1951) points out, more and more attention is being focused on the disturbance of vitamin A metabolism in diseases of the liver, which has been

shown by Moore (1931) to store about 95 per cent. of the vitamin A reserve. Keratomalacia has been recorded in association with hepatic disease, by early workers (Hori, 1895; Elschnig, 1899), and by Bloch (1924), Blegvad (1924), Jeghers (1937), and Haig, Hecht, and Patek (1938). Investigators working for the Medical Research Council (1949) found that the only useful criteria of vitamin A deficiency were the plasma level of vitamin A and the dark-adaptation values. Delayed dark adaptation (Haig and Patek, 1942; Patek and Haig, 1939; Haig and others, 1938), low plasma vitamin A (Harris and Moore, 1947; Popper, Steigmann, and Zevin, 1943; Haig and others, 1942), and slight response to vitamin A in tolerance curves (Popper and others, 1943) are found in cases of hepatic disease. The concentration of vitamin A in the liver was found to be reduced in six cases of cirrhosis (Haig and Patek, 1942), but was discovered to be within normal limits (900 international units/g.) in a case of acute yellow atrophy, in spite of a reduced plasma vitamin A level of only 19 international units per 100 ml. shortly before death (Harris and Moore, 1947).

A study of the literature leaves no doubt that lack of vitamin A may result from hepatic disease, and experimental and clinical evidence supports the view that vitamin A deficiency may be a potential cause of retinitis pigmentosa. It is therefore conceivable that the patient described above may have developed retinitis pigmentosa as the result of vitamin A deficiency secondary to defective hepatic function. The plasma vitamin A value of 105·5 units per 100 ml., which is the lower limit of normal (Bicknell and Prescott, 1946), may be against the theory of vitamin A deficiency, but this figure is lower than the mean normal figure of 121 international units (from estimates on 195 subjects by Medical Research Council, 1949) and the average of 118 international units found in 41 healthy adults by Leitner and Moore (1946). Yudkin (1941) found no standard level of blood vitamin A which can be used as a test for deficiency. The Medical Research Council (1949) showed that no great reliance could be placed on the results of a single estimation of vitamin A in plasma, the values obtained by three different laboratories often varying for the same sample, though the average of a sufficient number yielded consistent results. Harris and Moore (1947) concluded, from investigations on infective hepatitis, that the various mechanisms concerned with the metabolism of vitamin A (its absorption from the intestines, its deposition in the liver, its release from the liver to the plasma, and possibly its stability suffering to varying extents in different individuals) are not always equally affected. Thus, inability of the liver to remove vitamin A from the blood would allow it to pile up to a high level.

The slight response of my patient to vitamin A therapy could be explained by a severe degree of irrecoverable retinal destruction. Patients with cirrhosis of the liver (Patek and Haig, 1939) and even normal subjects receiving a low vitamin A intake (Hecht and Mandelbaum, 1938) may exhibit a sluggish response to vitamin A administration.

Summary

A case of retinitis pigmentosa associated with Gaucher's disease is described. The symptoms of retinitis pigmentosa did not develop until the age of 22 years. The patient showed evidence of defective liver function.

The suggestion has been made that the retinitis pigmentosa may have been caused by deficiency of vitamin A resulting from failure of liver function.

An interesting point, unconnected with the title of this paper, is the patient's statement that he took much longer than other individuals to recover from attacks of malaria, his lack of resistance being perhaps due to the splenectomy operation performed in childhood.

I wish to express my gratitude to Dr. W. G. S. Hopkirk for his radiological investigations, to Mr. A. W. Pearson and the late Brig. R. P. Cormack for the pathological reports, and to Dr. J. R. Gregory and Dr. L. Hirsch for their kind co-operation.

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APPLIANCE

A NEW SUTURE NEEDLE FOR CORNEAL SURGERY*

BY

C. A. PITTAR

Auckland, New Zealand

IT occurred to me some time ago that, if one used a straight needle so that in placing sutures there was no bending force applied by the needle-holder, this needle could be greatly reduced in diameter. This smaller cross-section would in turn allow it to penetrate tough tissue such as the cornea much more easily.

Further, I felt that with a straight needle one could place sutures much more accurately in that one could gauge the point of exit more exactly. For instance, in direct suturing of corneal grafts, one wants to introduce the needle near the edge of the epithelial surface and to bring it out on the cut edge of the graft. It must not go through to the endothelial surface nor must it take too shallow a bite. With the normal curved needle this can be quite difficult to gauge, but with a straight needle the angle is easy to judge in order to bring it out at the correct depth. There is also no risk of this needle cutting out as there is with a curved needle going shallow.

I therefore had a straight needle made from 15-gauge wire material which has a diameter of only 0·010 inches. It was 4 mm. long, triangular pointed, and flattened at the other end for the eye. For comparison it may be noted that the ordinary No. 6 curved eye needle is made from 10-gauge and the standard Jameson Evans corneal needle from 12-gauge wire (Evans, 1954).

I have given these needles an extended trial for 8 or 9 months, using them particularly for suturing penetrating corneal grafts and for edge-to-edge suturing of cataract sections. I have also used Jameson Evans and Griesshaber needles during this period for comparison. In some corneal grafts with multiple sutures, I have put in some sutures with the straight and some with the curved needles in the same case.

I have found the straight needles very satisfactory for the following reasons:

(1) They penetrate the cornea more easily and cause much less trauma.

(2) There is less tendency for the sutures introduced by them to cut out than for those introduced by curved needles. This has been proved in corneal grafts in which both types of needle have been used and sutures left in for up to 28 days.

(3) They can be placed more accurately, and being so short they can be pulled through without difficulty and with no danger of injuring underlying structures

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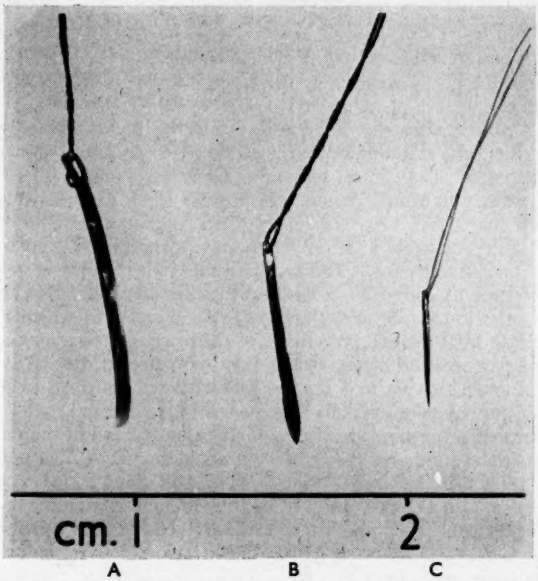
such as the lens. In placing them in the recipient cornea of an eye being grafted, the cornea can be raised sufficiently to make their insertion quite safe.



A. No. 6 eye curved needle. B. Jameson Evans needle. C. Straight needle. (The thread on the two curved needles is 6/0 silk.) ×4.

The disadvantages of these needles as compared with the more conventional curved needles are small, and may be summed up as follows:

(1) Because of their very small size threading them may be difficult without a binocular loupe. For all practical purposes the largest thread that will go through the needle is 6/0 silk or catgut. For corneal grafting I have been using some monofilament material so fine that it is not only easy to thread but falls out if not tied on to the needle. It is however so fine that the knot offers no obstruction at all.

(2) The needle may sometimes tend to turn sideways in the needle-holder if during the insertion the pressure is not kept directly in its long axis. This is largely overcome by using a very accurate needle-holder and gripping the needle close to the flattened end. I use a Barraquer needle-holder with no serrations on the jaws which I find very satisfactory.

(3) So far these needles have only been made from carbon steel, as stainless steel was not available in this gauge at the time. If this can be obtained in the future it should be used in preference to avoid rusting.

I am greatly indebted to the principals of Shrimpton and Fletcher Ltd., Redditch, England, for their help and advice in designing and making these needles.

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BOOK REVIEW

Is Diabetes a Vascular Disease? (Der Diabetes mellitus ein Gefäss-Problem?) By R. THIEL. Suppl. 25 to *Klin. Mbl. Augenheilk.*, 1956. Pp. 58, 35 figs. Enke, Stuttgart.

Though Thiel does not answer his question directly, he undoubtedly considers that vascular changes and the resulting asphyxia of the tissue are the essential features of the pathology of diabetes. The clinical picture of diabetic retinopathy is illustrated by excellent colour plates. In young patients the disease leads to massive neoformation of capillaries which may form a *rete mirabile*. Thiel suggests the name "rubeosis retinae diabetica". Histological sections show the damage done to the capillary walls and the development of microaneurysms. The capillaries are not the only vessels to be affected. While deposits of lipoids and glyco-proteins in the capillary walls may be found in other conditions (*e.g.* arteriosclerosis and glaucoma), the manner in which these substances affect the vessels and the relative percentage of their occurrence are typical for diabetes. Thiel stresses the part which is played by the muco-polysaccharides. The reviewer misses reproductions of analogous sections stained by Sudan red and PAS to show the participation of lipoids and glyco-proteins in these degenerative changes.

Becker's experiments on the dependence of diabetic changes in the retina and the co-ordinated intercapillary glomerulo-sclerosis on an increased ACTH activity are briefly mentioned.

The deposits diminish the permeability of the vascular membrane, a result which is enhanced by ionic disturbance and latent acidosis, which in turn promote the precipitation of glyco-proteins. Cortisone and ACTH act adversely by inducing sodium and water retention while potassium is lost. Insulin can also cause vascular damage by changing the ionic environment and especially by developing antigen properties, leading to allergic injury of the capillaries.

After reading Thiel's contribution, an ophthalmologist may feel overawed by the multiplicity and intricacy of the factors involved in the diabetic problem. It appears that a thorough knowledge of physical and organic chemistry, and of the metabolism of the diabetic tissue is required for an understanding of the pathology of diabetes.

NOTES

CORNEO-PLASTIC UNIT AND REGIONAL EYE BANK

Queen Victoria Hospital, East Grinstead, Surrey

During 1957 a series of demonstration discussions will be held to illustrate the relationship of ophthalmology and plastic surgery. These meetings will commence at 2 p.m. on a Saturday and will include a short lecture, illustrative operations, examination of patients, films, and discussion.

The subjects for study will be: Keratoplasty; Ptosis; Surgery of lacrimation; Reconstruction of the conjunctival fornices, socket, and orbit; and Treatment of positional and paretic diplopia.

The first meeting, to be held on January 19, 1957, will deal with keratoplasty. These demonstrations are without fee, and numbers will be limited to twelve surgeons per session. Applications should be made to the Secretary, Corneo-Plastic Unit and Regional Eye Bank, Queen Victoria Hospital, East Grinstead (Tel: East Grinstead 987).

WILLS EYE HOSPITAL, PHILADELPHIA

The IX Annual Clinical Conference of the Staff and Society of Ex-Residents of Wills Eye Hospital will be held at the hospital on February 8 and 9, 1957. The Conference this year will be of especial interest since it will be an important feature in commemorating the 125th anniversary of the founding of the hospital.

The Bedell Lecture will be delivered by Dr. John M. McLean of New York City on the subject of "Management of the Primary Glaucomas".

The programme will also include scientific papers by members of the staff and ex-residents of the hospital, technical exhibits, and a colour television programme sponsored by Smith, Kline, and French Laboratories.

On completion of the two-day programme, the Wills Eye Hospital Society will hold its annual meeting and dinner at the Union League, Philadelphia.

Before the Conference on February 7, there also will be a meeting, preceded by dinner, of the Ophthalmological Section of the College of Physicians in Philadelphia. Dr. James H. Allen of New Orleans will be the guest speaker. All ophthalmologists are invited.

OBITUARY

VLADIMIR PETROVICH FILATOV

(1875–1956)

The ophthalmological world will regret that Vladimir Petrovich Filatov died in Odessa on October 31, 1956, at the age of 81. He was born in Saransk in the Ukraine on February 15, 1875, and graduated in medicine in Moscow in 1897 where he held his first hospital appointments. In 1908 he went to Odessa where he eventually became the Director of the Ophthalmological Institute; here he worked until the time of his death, the latter part of his life being spent as Director of the Ukrainian Experimental Institute for Eye Diseases and Tissue Therapy.

In addition to his ophthalmological work, which embraced many aspects of our specialty, he took a considerable interest in general medicine and was also a deputy of the Ukrainian Supreme Soviet. He was undoubtedly one of the great ophthalmologists of our generation, and many of us in Great Britain have regretted the fact that closer contact with him and a more personal appreciation of his ideas have been impossible.

In ophthalmology his greatest contribution was in the biology of corneal grafts and the perfecting of the surgical techniques of keratoplasty. It will be remembered that von Hippel of Göttingen was the pioneer who, towards the end of the last century, made this operation a clinical possibility. Filatov shares with Elschnig of Prague the distinction of evolving the technique to make the operation a practical surgical procedure. As early as 1913 he was experimenting on the feasibility of total corneal grafting, transplanting the entire cornea with a margin of sclera and conjunctiva. This drastic procedure, of course, gives no clinical results of value, but the attempt illustrates his courage as a surgical enthusiast.

There are two big advances with which his name is associated in connexion with corneal grafts. The first of these concerns the use of cadaver eyes. Some time previously Magitot of Paris had shown that a graft could be preserved for a period varying from one to two weeks at a low temperature in haemolysed blood. With this as basis Filatov went further and popularized the use of grafts removed from cadaver eyes which, as early as 1934, he was using 41 hours after death. This, of course, opened up a vast source of graft material and is universally practised to-day with great benefit.

The second great advance he made was in the employment of lamellar grafts not for visual purposes but with a view to obtaining a suitable bed for a final graft. In the previous century von Hippel had practised lamellar keratoplasty and Elschnig in the

early 1920s had demonstrated that a corneal graft would take only if there were a sufficiency of clear cornea in the eye of the recipient; a graft inserted into a bed of corneal scar tissue invariably turned opaque. In such a cornea Filatov inserted a clear lamellar graft and at a later stage inserted a penetrating graft for visual purposes.

In work such as this he noticed that the implantation of a graft tended to clear corneal opacities which might already be present. Upon this observation he built up a theory of the stimulation of tissues by the release of "biogenic substances", a theory which became a considerable cult in Russian medicine. With this as the theoretical basis, he launched a new method of therapy based on the injection, topically or systemically, of a vast number of animal and vegetable substances, the products of which were assumed to stimulate the tissues of the host, and for a time this method of "tissue therapy" was widely employed in the treatment of a host of degenerative ocular diseases which responded to no other therapy—myopic chorio-retinal atrophy, primary pigmentary degeneration of the retina, optic atrophy, and so on. The most common material ultimately employed was derived from the placenta which was used either as the injection of placental extract or the subconjunctival implantation of placental tissue. Most ophthalmologists are agreed that whatever the theoretical justification for this method of therapy, in practice it brought little or no benefit, and it has generally fallen completely out of use. However this may be, Filatov will always be remembered for his achievements in technical surgery and the originality of his concepts.

R. C. J. MEYER

Reinhard Carl Johannes Meyer, who died on November 7, 1956, in Johannesburg, was born in 1883 in Kimberley, Cape Province, South Africa. He was the son of a missionary, and was educated in Kimberley and in Cape Town, where he graduated B.A. in 1902. He was awarded the Jamieson Scholarship and took a medical training at Edinburgh University where he graduated M.B., Ch.B. in 1908.

He returned to South Africa to become house physician and house surgeon at the Johannesburg General Hospital from 1910 to 1912. In 1953 he returned to Europe for further studies, taking his M.D. and F.R.C.S. at Edinburgh, and his D.O. at Oxford.

After demobilization from World War I he became a house surgeon at Moorfields Eye Hospital (R.L.O.H.), and he returned to South Africa in the latter part of 1919 to begin practice as an ophthalmic surgeon in Johannesburg. He was appointed ophthalmic surgeon to the Transvaal Memorial Hospital for Children in 1923 and to the staff of the Johannesburg General Hospital in 1924, where he served for a first term of 15 years. He was recalled to the Johannesburg General Hospital for the years 1939–1945 during the absence of other senior ophthalmic surgeons on war service.

In 1930, together with the late Dr. Wood of Cape Town and Dr. Verwey of Pietermaritsburg, he was instrumental in forming the Ophthalmological Society of South Africa, of which he became President in the years 1938 and 1939.

He was one of the pioneers in South Africa of diathermy treatment for detachment in the early 1930s, of intra-capsular extractions of cataracts about the same time, and of corneal grafting in 1937.

He took a keen interest in the work of the Society to help the civilian blind in Johannesburg, and was associated from the inception with the St. John Ophthalmic Foundation which established an Eye Hospital on the outskirts of Johannesburg to begin work in 1951.

He was married in Bournemouth in 1916 to Phyllis Bagshaw who survives him, as do also his only daughter, and three sons who are members of the medical profession.